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Set	Items	Description
S8	880	(ETEC OR (ENTEROTOX? OR ENTERO(W)(TOXIGEN? OR TOXI???))(5N-)COLI)(5N)DIARRH?
S9	117	S8 AND (CFA?? OR COLON?(W)FACTOR(W)ANTIGEN? ?)
S10	51	S9 AND (VACCIN? OR IMMUNIS? OR IMMUNIZ?)
S11	24	S10 AND (MOUTH OR ORAL? OR PER(W)OS)
S12	54	S9 AND (LT OR HEAT(W)LABILE)
S13	68	S11 OR S12
S14	46	RD (unique items)

- key Terms

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14/3,AB/1 (Item 1 from file: 35)
DIALOG(R)File 35:Dissertation Abs Online
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01700021 AAD9927545
RELATIONSHIP BETWEEN *ENTEROTOXIGENIC"** ESCHERICHIA *COLI"** AND TRAVELERS' *DIARRHEA"** IN MEXICO, FROM 1992 TO 1997
Author: JIANG, ZHI-DONG
Degree: DR.P.H.
Year: 1998
Corporate Source/Institution: THE UNIV. OF TEXAS H.S.C. AT HOUSTON SCH. OF PUBLIC HEALTH (0219)
Source: VOLUME 60/04-B OF DISSERTATION ABSTRACTS INTERNATIONAL. PAGE 1425. 79 PAGES

The purpose of this study was to examine the relationship between enterotoxigenic *ETEC"** and travelers' *diarrhea"** over a period of five years in Guadalajara, Mexico. Specifically, this study identified and characterized *ETEC"** from travelers with *diarrhea"**. The objectives were to study the *colonization"** *factor"** *antigens"**, toxins and

antibiotic sensitivity patterns in ETEC from 1992 to 1997 and to study the molecular epidemiology of ETEC by plasmid content and DNA restriction fragment patterns.

In this survey of travelers' diarrhea in Guadalajara, Mexico, 928 travelers with diarrhea were screened for enteric pathogens between 1992 and 1997. ETEC were isolated in 195 (19.9%) of the patients, representing the most frequent enteric pathogen identified.

A total of 31 antimicrobial susceptibility patterns were identified among ETEC isolates over the five-year period.

The 195 ETEC isolates contained two to six plasmids each, which ranged in size from 2.0 to 23 kbp.

Three different reproducible rRNA gene restriction patterns (ribotypes R-1 to R-3) were obtained among the 195 isolates with the enzyme, <italic> Hind</italic>III.

*Colonization"** *factor"** *antigens"** (*CFAs"**) were identified in 99 (51%) of the 195 ETEC strains studied.

Cluster analysis of the observations seen in the four assays all confirmed the five distinct groups of study-year strains of ETEC. Each group had a >95% similarity level of strains within the group and &*lt"** ;60% similarity level between the groups. In addition, discriminant analysis of assay variables used in predicting the ETEC strains, reveal a >80% relationship between both the plasmid and rRNA content of ETEC strains and study-year.

These findings, based on laboratory observations of the differences in biochemical, antimicrobial susceptibility, plasmid and ribotype content, suggest complex epidemiology for ETEC strains in a population with travelers' diarrhea. The findings of this study may have implications for our understanding of the epidemiology, transmission, treatment, control and prevention of the disease. It has been suggested that an ETEC vaccine for humans should contain the most prevalent *CFAs"**. Therefore, it is important to know the prevalence of these factors in ETEC in various geographical areas.

*CFAs"** described in this dissertation may be used in different epidemiological studies in which the prevalence of *CFAs"** and other properties on ETEC will be evaluated. Furthermore, in spite of an intense search in near 200 ETEC isolates for strains that may have clonal relationship, we failed to identify such strains. However, further studies are in progress to construct suitable live vaccine strains and to introduce several of *CFAs"** in the same host organism by recombinant DNA techniques (Dr. Ann-Mari Svennerholm's lab). (Abstract shortened by UMI.)

14/3,AB/2 (Item 2 from file: 35)
DIALOG(R)File 35:Dissertation Abs Online

01646925 AAD9833003
THE EPIDEMIOLOGY OF *ETEC"** *DIARRHEA"** AND ASSOCIATION OF *DIARRHEA"** AND MALNUTRITION IN A COHORT OF YOUNG EGYPTIAN CHILDREN

Author: WIERZBA, THOMAS FREDRICK
Degree: PH.D.
Year: 1998
Corporate Source/Institution: THE JOHNS HOPKINS UNIVERSITY (0098)
Source: VOLUME 59/05-B OF DISSERTATION ABSTRACTS INTERNATIONAL.
PAGE 2160. 173 PAGES

We studied the distribution, pathogenicity and virulence of *enterotoxigenic"** E. *coli"** *diarrhea"** and the association between

*diarrhea"** and malnutrition in a cohort of children aged less than three years from a periurban area of Egypt. Home visits were made to each household twice weekly from Nov. 1993 to Sept. 1995. Clinical data and rectal swabs were obtained from each child with a loose stool. Fecal specimens were collected once a month from non-diarrheal participants. Anthropometric measurements were made at three month intervals. E. coli colonies were tested for *heat"** *labile"** (*LT"**) and heat stable (ST) toxin and *colonization"** *factor"** *antigens"** (*CFAs"**). A diarrhea episode was defined as three or more loose or watery stools or one bloody stool in a 24 hour period.

Among 242 children, diarrhea incidence was 2.9 episodes per year (epy), while ETEC was 0.6 epy. Children $<$12, 12-23 and 24-35 months had an ETEC incidence of 1.0, 0.6 and 0.1 epy, respectively. Twenty-three percent of ETEC expressed a known *CFA"**. ST-ETEC incidence was 2.5 times more common in the warmer than cooler months, while *LT"**-ETEC showed no seasonality. ETEC incidence increased when a garbage container was present in the house (RR = 1.5) and in crowded households. The presence of a sanitary latrine was protective (RR = 0.5). ST-ETEC, but not *LT"**-ETEC, were more frequently isolated from cases than controls for children less than two years old. Twenty-four percent of cases reported vomiting and physicians reported dehydration in 16% of cases.

Among 143 children included in the nutrition study, 358 diarrheal episodes were reported, 1% of which lasted $\ge$14 days. Stunting, wasting and low weight-for-age were documented in 19%, 3% and 7%, respectively. An association was detected between greater than or equal to two diarrhea episodes and subsequent changes in weight-for-age ($-$0.24 Z-score) and height for age ($-$0.28 Z-scores) occurring over approximately three month intervals. This association did not hold, however, when analyzed over six month intervals if no diarrhea was reported in either the first or second half of this interval. When testing whether malnutrition predisposes to diarrhea, weight-for-age ${<}\ {-}$2 Z-scores among the poorest children was associated with diarrhea (RR = 1.8). Diarrhea itself was also associated with a subsequent attack (RR = 1.9).

In this nominally well off population, *diarrhea"** is moderately high with *ETEC"** representing 20% of all episodes. The results suggest that ETEC epidemiology differs by toxin; ST-ETEC is more pathogenic and more frequent during warm months than *LT"**-ETEC. Improved sanitation could reduce *ETEC"** incidence. *Diarrhea"** does not appear to substantially contribute to malnutrition when these children had diarrhea free time for catch up growth. Low weight-for-age among the poor and diarrhea itself was associated with subsequent risk of diarrhea.

14/3,AB/3 (Item 3 from file: 35)
DIALOG(R)File 35:Dissertation Abs Online

01285658 AADC282978
ENTEROTOXIGENIC, NECROTIZING AND VEROTOXIGENIC ESCHERICHIA COLI OF HUMAN AND BOVINE ORIGIN (ENTEROTOXIGENICITY, VEROTOXIGENICITY)
Original Title: ESCHERICHIA COLI ENTEROTOXIGENICOS, NECROTIZANTES Y VEROTOXIGENICOS DE ORIGEN HUMANO Y BOVINO

Author: BLANCO ALVAREZ, MIGUEL
Degree: DR.
Year: 1991
Corporate Source/Institution: UNIVERSIDAD DE SANTIAGO DE COMPOSTELA (SPAIN) (5869)

Source: VOLUME 54/02-C OF DISSERTATION ABSTRACTS INTERNATIONAL.
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ISBN: 84-7191-800-5
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UNIVERSIDADE DE SANTIAGO DE COMPOSTELA, SANTIAGO, SPAIN

We have established the existence of two types of cytotoxic necrotizing factor (CNF1 and CNF2) produced by animal and clinical isolates of necrotizing Escherichia coli (NTEC) (114). CNF1 is produced by E. coli that cause extraintestinal infections in humans (10), whereas CNF2 is elaborated by bovine strains isolated from calves with diarrhoea or septicaemia and from healthy controls.

To assess the role of enterotoxigenic (ETEC), verotoxigenic (VTEC) and necrotizing (NTEC) E. coli in infantile and bovine diarrhoea, 482 children and 197 calves with diarrhoea and 215 (103 children and 112 calves) healthy controls, from differents localities of Galicia, north western Spain, were investigated between 1985 and 1991. ETEC were significantly more frequently isolated from children with diarrhoea who were under one month of age (26%) than from older diarrhoeic children (2%) (P $<$ 0,001) or from healthy children who were under one month of age (0%) (P $<$ 0,05). Most human *ETEC"** isolates from sporadic cases of *diarrhoea"** belonged to serotypes O153:K-:H45 (9 STa$\sp{+}$*CFA"**/I$\sp{+}$ strains), O27:K-:H7 (3 STa$\sp{+}$PCFO27$\sp{+}$) or O6:K15:H16 (2 *LT"**$\sp{+}$STa$\sp{+}$ *CFA"**/II$\sp{+}$). NTEC strains CNF1$\sp{+}$ were isolated in similar proportion from the stools of children with diarrhoea (20%) than from healthy controls (19%) (P $<$ 0,98). VTEC strains only were isolated from 3 (0,6%) diarrhoeic children and it belonged to serotypes O26:H11 (2 cases) and O86:H10.

ETEC STa$\sp{+}$K99$\sp{+}$ was isolated from 1 (0,5%) of 197 calves with diarrhoea and from 3 (3%) of 112 healthy controls (P $<$ 0,3). In contrast, VTEC and NTEC CNF2$\sp{+}$ were detected in 9% and 20% diarrhoeic calves versus 19% (P $<$ 0,05) and 34% (P $<$ 0,01) in healthy controls. These results suggest that VTEC and NTEC strains may be components of the normal intestinal flora of calves. Serogroups to which VT-producing strains belonged differed considerably from the serogroups determined in CNF2-producing strains and the remaining E. coli strains isolated in this study. Four new surface antigens associated with MRHA$\sp{+}$ E. coli strains were identified. Vir and B23 surface antigens were more frequently detected in CNF2-producing strains than in CNF2 negative strains. NTEC bovine strains of serotype O55:H21 expressed the Vir pilus, whereas CNF2$\sp{+}$ O55:H4 strains were positives for P fimbria characteristic of pyelonephritic E. coli of human origin. (Abstract shortened by UMI.)

838666 AAD8405464
CHARACTERIZATION OF THE *COLONIZATION"** *FACTOR"** *ANTIGEN"** II PLASMID (*CFA"**/II) FROM ENTEROTOXIGENIC ESCHERICHIA COLI

Author: PENARANDA, MARIA ELENA

Degree: PH.D.
Year: 1983
Corporate Source/Institution: THE UNIV. OF TEXAS H.S.C. AT HOUSTON GRAD. SCH. OF BIOMED. SCI. (2034)
Source: VOLUME 44/12-B OF DISSERTATION ABSTRACTS INTERNATIONAL.
PAGE 3661. 182 PAGES

The etiological role of *enterotoxigenic"** E. *coli"** (*ETEC"**) in *diarrheal"** diseases of man and domestic animals is firmly established. Besides the production of enterotoxins (ST and *LT"**), ETEC produces other important virulence factors; the *colonization"** *factor"** *antigens"** (*CFAs"**). *CFAs"** mediate the attachment of ETEC to the epithelial cells of the small intestine, and this favors colonization by the bacteria and facilitates delivery of the enterotoxins to the intestinal cells.

The production of enterotoxin and *CFA"** is determined by plasmids and has been found to be restricted to a select number of E. coli serotypes.

In this work, plasmid DNA analysis was performed in twenty-three *CFA"**/II-producing enterotoxigenic Escherichia coli strains and their spontaneous *CFA"**/II-negative derivatives. In some cases, strains lost the high molecular weight plasmid and also the ability to produce *CFA"** /II, ST and *LT"**. In other cases there was a deletion of the plasmid, which produced strains that were *CFA"**/II('-), ST('-), *LT"**('-) or *CFA"**/II('-), ST('+), *LT"**('+).

The *CFA"**/II plasmid from strain PB-176 (06:H16:*CFA"**/II('+), ST('+), *LT"**('+)) was transferred by transformation into E. coli K12 with concomitant transfer of the three characteristics: *CFA"**/II, ST and *LT"**.

A physical map of the prototype *CFA"**/II:ST:*LT"** (pMEP60) plasmid was constructed by restriction endonuclease analysis and compared to plasmids from three other *CFA"**/II-producing strains. A *CFA"** /II-negative (but ST and *LT"** positive) deletion derivative of pMEP60 (pMEP30) was also included in the map. The four *CFA"**/II plasmids analyzed had a common region of approximately 30 kilobase pairs. The toxin genes were approximately 5 kbp apart and about 20 kbp from the common region. The information given by this physical map could be of great value when constructing a clone that will express the *CFA"**/II genes but not the toxin genes.

14/3,AB/5 (Item 1 from file: 144)
DIALOG(R)File 144:Pascal

15272774 PASCAL No.: 01-0443053
Toxins and *colonization"** *factor"** *antigens"** of enterotoxigenic Escherichia coli among residents of Jakarta, Indonesia
OYOFO Buhari A; SUBEKTI Decy S; SVENNERHOLM Ann-Mari; MACHPUD Nunung N; TJANIADI Periska; KOMALARINI S; SETIAWAN Budhi; CAMPBELL James R; CORWIN Andrew L; LESMANA Murad
United States Naval Medical Research Unit No. 2, Jakarta, Indonesia; Department of Medical Microbiology and Immunology, University of Goteburg, Sweden; Sumber Warns Hospital, Jakarta, Indonesia; Friendship Hospital, Jakarta, Indonesia
Journal: The American journal of tropical medicine and hygiene, 2001, 65 (2) 120-124
Language: English
Infection caused by enterotoxigenic Escherichia coli (ETEC) poses a serious health problem among children and adults in developing countries. Colonization of the small intestinal mucosa by ETEC strains is mediated by antigenically specific fimbriae, also known as *colonization"** *factor"** *antigens"** (*CFA"**). The significance of this study arises from reports that active and passive immunization with ETEC strains harboring *CFAs"**

has previously been shown to induce protective immunity against diarrhea in animal models. The aim of this study was to determine toxin-associated *CFAs"** of *ETEC"** isolated from a *diarrheal"** disease case-control study in Jakarta, Indonesia. Thirteen hundred and twenty-three diarrheic and control patients with lactose-fermenting colonies were screened by ganglioside GM1-enzyme-linked immunosorbent assay (GM1-ELISA) for *heat"**-*labile"** (*LT"**) and heat-stable (ST) toxins. Two hundred and forty-six (19%) ETEC isolates identified by GM1-ELISA for the *LT"**/ST toxins were screened for *CFAs"** by Dot blot assay using monoclonal antibodies against *CFA"** /I, II, and IV and against the putative colonization antigens (PCF) PCFO159, PCFO166, CS7, and CS17. Of the 246 ETEC isolates, 177 (72%) elaborated ST, 56 (23%) produced *LT"**, while 13 (5%) elicited both the ST and *LT"** toxins. *CFA"** testing of the 246 ETEC isolates showed that 21 (8%) expressed *CFA"**/I, 3 (1%) exhibited *CFA"**/II, 14 (6%) elaborated *CFA"**/IV, while 7 (3%) expressed PCFO159 and PCFO159 plus CS5. No *CFAs"** or PCFs could be associated with 201 (82%) of the ETEC strains. This report documents the types of *CFAs"** associated with ETEC strains in Jakarta, Indonesia. These data may help current research efforts on the development of *CFA"**-based vaccines for humans against ETEC and provide additional information for future ETEC vaccine trials in Southeast Asia.

14/3,AB/6 (Item 2 from file: 144)
DIALOG(R)File 144:Pascal

14960832 PASCAL No.: 01-0113499
Human antibody response to Longus type IV pilus and study of its prevalence among enterotoxigenic Escherichia coli in Bangladesh by using monoclonal antibodies
QADRI F; GIRON J A; HELANDER A; BEGUM Y A; ASADUZZAMAN M; XICOHTENCATL-CORTES J; NEGRETE E; ALBERT M J
International Centre for Diarrhoeal Disease Research, Bangladesh (ICDDR.B), Dhaka, Bangladesh; Centro de Investigaciones en Ciencias Microbiologicas, Benemerita Universidad Automoma de Pucbla, Puehla, Mexico; Department of Medical Microbiology and Immunology, Goeteborg University, Goeteborg, Sweden
Journal: The Journal of infectious diseases, 2000, 181 (6) 2071-2074
Language: English
Mouse monoclonal antibodies (MAbs) were derived against longus (CS20), a type IV pilus expressed by human enterotoxigenic Escherichia coli (ETEC). One MAb (ICA39) detected longus in 56 (8.5%) of 662 ETEC isolates obtained from a routine surveillance of diarrheal stools from children and adults. Five patients with *diarrhea"** from whom longus-positive *ETEC"** were isolated were also recruited. Of these 61 isolates, 50 were positive for other colonization factors (CFs; 61% for *CFA"**/II and 21% for *CFA"**/I), and 11 were negative for any of the other 8 CFs that were tested. They were either positive for the heat-stable enterotoxin (ST; n = 29) or for the *heat"**-*labile"** enterotoxin (*LT"**) and ST (n = 32). All longus-positive ETEC were confirmed by polymerase chain reaction to harbor IngA, the longus structural pilin gene. Sera andlor fecal extracts from the patients reacted with the 22-kDa pilin polypeptide in immunoblots and ELISA. These studies show that longus is prevalent among ETEC in Bangladesh and that longus gives rise to IgA antibody responses in patients.

14/3,AB/7 (Item 3 from file: 144)
DIALOG(R)File 144:Pascal

14420201 PASCAL No.: 00-0077137
Characterization of an enterotoxigenic Escherichia coli strain from Africa expressing a putative colonization factor
KHALIL S B; CASSELS F J; SHAHEEN H I; PANNELL L K; EL-GHORAB N; KAMAL K; MANSOUR M; SAVARINO S J; PERUSKI L F JR
Research Sciences Department, U.S. Naval Medical Research Unit No. 3, Cairo, Egypt; Department of Enteric Infections, Division of Communicable Diseases and Immunology, Walter Reed Army Institute of Research, Washington, D.C. 20307-5100, United States; Structural Mass Spectrometry Group, National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health, Bethesda, Maryland 20892, United States
Journal: Infection and immunity, 1999, 67 (8) 4019-4026
Language: English
An enterotoxigenic Escherichia coli (ETEC) strain of serotype O114:H- that expressed both *heat"**-*labile"** and heat-stable enterotoxins and tested negative for colonization factors (CF) was isolated from a child with diarrhea in Egypt. This strain, WS0115A, induced hemagglutination of bovine erythrocytes and adhered to the enterocyte-like cell line Caco-2, suggesting that it may elaborate novel fimbriae. Surface-expressed antigen purified by differential ammonium sulfate precipitation and column chromatography yielded a single protein band with M SUB r 14,800 when resolved by sodium dodecyl sulfate-polyacrylamide gel electrophoresis (16% polyacrylamide). A monoclonal antibody against this putative fimbrial antigen was generated and reacted with strain WS0115A and also with CS1-, CS17-, and CS19-positive strains in a dot blot assay. Reactivity was temperature dependent, with cells displaying reactivity when grown at 37 Degree C but not when grown at 22 Degree C. Immunoblot analysis of a fimbrial preparation from strain WS0115A showed that the monoclonal antibody reacted with a single protein band. Electron microscopy and immunoelectron microscopy revealed fimbria-like structures on the surface of strain WS0115A. These structures were rigid and measured 6.8 to 7.4 nm in diameter. Electrospray mass-spectrometric analysis showed that the mass of the purified fimbria was 14,965 Da. The N-terminal sequence of the fimbria established that it was a member of the *CFA"**/I family, with sequence identity to the amino terminus of CS19, a new CF recently identified in India. Cumulatively, our results suggest that this fimbria is CS19. Screening of a collection of *ETEC"** strains isolated from children with *diarrhea"** in Egypt found that 4.2% of strains originally reported as CF negative were positive for this CF, suggesting that it is biologically relevant in the pathogenesis of ETEC.

14/3,AB/8 (Item 4 from file: 144)
DIALOG(R)File 144:Pascal

14263870 PASCAL No.: 99-0467647
Phenotypic diversity of enterotoxigenic Escherichia coli strains from a community-based study of pediatric diarrhea in periurban Egypt
PERUSKI L F JR; KAY B A; EL-YAZEED R A; EL-ETR S H; CRAVIOTO A; WIERZBA T

F; RAO M; EL-GHORAB N; SHAHEEN H; KHALIL S B; KAMAL K; WASFY M O; SVENNERHOLM A M; CLEMENS J D; SAVARINO S J

U.S. Naval Medical Research Unit No. 3, Cairo, Egypt; Facultad de Medicina, Universidad Nacional Autonoma de Mexico, Mexico, D.F., Mexico; National Institute of Child Health and Human Development, Bethesda, Maryland, United States; Department of Medical Microbiology and Immunology, Goteborg University, Goteborg, Sweden

Journal: Journal of clinical microbiology, 1999, 37 (9) 2974-2978

Language: English

No past studies of diarrhea in children of the Middle East have examined in detail the phenotypes of enterotoxigenic Escherichia coli (ETEC) strains, which are important pathogens in this setting. During a prospective study conducted from November 1993 to September 1995 with 242 children under 3 years of age with diarrhea living near Alexandria, Egypt, 125 episodes of *diarrhea"** were positive for *ETEC"**. *ETEC"** strains were available for 98 of these episodes, from which 100 ETEC strains were selected and characterized on the basis of enterotoxins, colonization factors (CFs), and O:H serotypes. Of these representative isolates, 57 produced heat-stable toxin (ST) only, 34 produced *heat"**-*labile"** toxin (*LT"**) only, and 9 produced both *LT"** and ST. Twenty-three ETEC strains expressed a CF, with the specific factors being CF antigen IV (*CFA"**/IV; 10 of 23; 43%), *CFA"**/II (5 of 23; 22%), *CFA"**/I (3 of 23; 13%), PCF0166 (3 of 23; 13%), and CS7 (2 of 23; 9%). No ETEC strains appeared to express *CFA"** /III, CS17, or PCF0159. Among the 100 ETEC strains, 47 O groups and 20 H groups were represented, with 59 O:H serotypes. The most common O serogroups were O159 (13 strains) and O43 (10 strains). O148 and O21 were each detected in five individual strains, O7 and O56 were each detected in four individual strains, O73, O20, O86, and O114 were each detected in three individual strains, and O23, O78, O91, O103, O128, and O132 were each detected in two individual strains. The most common H serogroups were H4 (16 strains), 12 of which were of serogroup O159; H2 (9 strains), all of which were O43; H18 (6 strains); H30 (6 strains); and H28 (5 strains); strains of the last three H serogroups were all O148. Cumulatively, our results suggest a high degree of clonal diversity of disease-associated ETEC strains in this region. As a low percentage of these strains expressed a CF, it remains possible that other adhesins for which we either did not assay or that are as yet undiscovered are prevalent in this region. Our findings point out some potential barriers to effective immunization against *ETEC"** *diarrhea"** in this population and emphasize the need to identify additional protective antigens commonly expressed by ETEC for inclusion in future vaccine candidates.

14/3,AB/9 (Item 5 from file: 144)
DIALOG(R)File 144:Pascal

14257359 PASCAL No.: 99-0460752

Prospective cohort study of enterotoxigenic Escherichia coli infections in argentinean children

VIBOUD G I; JOUVE M J; BINSZTEIN N; VERGARA M; RIVAS M; QUIROGA M; SVENNERHOLM A M

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Journal: Journal of clinical microbiology, 1999, 37 (9) 2829-2833

Language: English

In a follow-up study, enterotoxigenic Escherichia coli (ETEC) infections in 145 children from two communities located in northeastern Argentina were monitored for 2 years. The occurrence of diarrhea was monitored by weekly household visits. Of 730 fecal specimens collected, 137 (19%) corresponded to *diarrheal"** episodes. *ETEC"** was isolated from a significantly higher proportion of symptomatic (18.3%) than asymptomatic (13.3%) children (P = 0.04541). Individuals of up to 24 months of age were found to have a higher risk of developing *ETEC"** *diarrhea"** than older children (odds ratio (OR), 3.872; P = 0.00021). When the toxin profiles were considered, only heat stable enterotoxin (ST)-producing *ETEC"** was directly associated with *diarrhea"** (P = 0.00035). Fifty-five percent of the ETEC isolated from symptomatic children and 19% of the ETEC isolated from asymptomatic children expressed one of the colonization factors (CFs) investigated, i.e., CF antigen I (*CFA"**/I), *CFA"**/II, *CFA"**/III, and *CFA"** /IV; coli surface antigens CS7 and CS17; and putative CFs PCFO159, PCFO166, and PCFO20, indicating a clear association between *diarrhea"** and *ETEC"** strains that carry these factors (P = 0.0000034). The most frequently identified CFs were *CFA"**/IV (16%), *CFA"**/I (10%), and CS17 (9%). CFs were mostly associated with ETEC strains that produce ST and both *heat"**-*labile"** enterotoxin and ST. Logistic regression analysis, applied to remove confounding effects, revealed that the expression of CFs was associated with illness independently of the toxin type (OR, 4.81; P = 0.0003). When each CF was considered separately, CS17 was the only factor independently associated with illness (OR, 16.6; P = 0.0151). Most CFs (the exception was *CFA"**/IV) fell within a limited array of serotypes, while the CF-negative isolates belonged to many different O:H types. These results demonstrate that some CFs are risk factors for the development of *ETEC"** *diarrhea"**.

14/3,AB/10 (Item 6 from file: 144)

DIALOG(R)File 144:Pascal

13662290 PASCAL No.: 98-0369834

Intestinal immune responses to an inactivated *oral"** enterotoxigenic Escherichia coli *vaccine"** and associated immunoglobulin A responses in blood

AHREN C; JERTBORN M; SVENNERHOLM A M

Department of Medical Microbiology and Immunology, Goeteborg University, Goeteborg, Sweden; Department of Infectious Diseases, Goeteborg University, Goeteborg, Sweden

Journal: Infection and immunity, 1998, 66 (7) 3311-3316

Language: English

An inactivated *oral"** *enterotoxigenic"** Escherichia *coli"** (*ETEC"**) *vaccine"** against *ETEC"** *diarrhea"** was given to 25 adult Swedish volunteers. The *vaccine"** consisted of formalin-killed E. coli bacteria expressing the most common *colonization"** *factor"** *antigens"** (*CFAs"**), i.e., *CFA"**/I, -II, and -IV, and recombinantly produced cholera B subunit (CTB). Immunoglobulin A (IgA) antibody responses in intestinal lavage fluid to CTB and *CFAs"** were determined and compared with corresponding responses in stool extracts and serum as well as with

IgA antibody-secreting cell (ASC) responses in peripheral blood. Two doses of *vaccine"** induced significant IgA responses to the different *CFAs"** in lavage fluid in 61 to 87% of the *vaccinees"** and in stool in 38 to 81% of them. The most frequent responses were seen against *CFA"**/I. The magnitudes of the antibody responses against CTB and *CFA"**/I in stool correlated significantly (CTB, $P < 0.01$; *CFA"**/I, $P < 0.05$) with those in intestinal lavage. Intestinal lavage responses against *CFAs"** were best reflected by the ASC responses, with the sensitivity of the ASC assay being 80 to 85%, followed by stool (sensitivity of 50 to 88%) and serum antibody (sensitivity of 7 to 65%) analyses. CTB-specific immune responses were seen in >90% of the *vaccinees"** in all assays.

14/3,AB/11 (Item 7 from file: 144)
DIALOG(R)File 144:Pascal

13477534 PASCAL No.: 98-0174793
Safety and immunogenicity of an *oral"**, killed enterotoxigenic Escherichia coli-cholera toxin B subunit *vaccine"** in Egyptian adults
SAVARINO S J; BROWN F M; HALL E; BASSILY S; YOUSSEF F; WIERZBA T; PERUSKI L; EL-MASRY N A; SAFWAT M; RAO M; JERTBORN M; SVENNERHOLM A M; LEE Y J; CLEMENS J D
US Naval Medical Research Unit No. 3, Cairo, Egypt; Egyptian Ministry of Health, Benha, Egypt; National Institute of Child health and Human Development, National Institutes of Health, Bethesda, Maryland, United States; University of Goeteborg, Goeteborg, Sweden
Journal: The Journal of infectious diseases, 1998, 177 (3) 796-799
Language: English
Enterotoxigenic Escherichia coli (ETEC) is the leading cause of bacterial diarrhea in young children in developing countries. The safety and immunogenicity of a killed, *oral"** ETEC *vaccine"** consisting of whole cells plus recombinantly produced cholera toxin B subunit (rCTB) was evaluated in Egypt, which is endemic for *ETEC"** *diarrhea"** . Seventy-four healthy Egyptian adults (21-45 years old) were randomized and received two doses of the ETECIrCTB *vaccine"** (E003) or placebo 2 weeks apart. The frequency of adverse events after either dose did not differ by treatment group, and no severe adverse events were reported. After *vaccination"**, peripheral blood IgA B cell responses to CTB (100%) and to *vaccine"** *colonization"** *factor"** *antigens"** *CFAII"** (94%), CS4 (100%), CS2 (81%), and CSI (69%) were significantly higher than response rates for the placebo group. These favorable results in Egyptian adults indicate that the ETEC/rCTB *vaccine"** is a promising candidate for evaluation in younger age groups in this setting.

14/3,AB/12 (Item 8 from file: 144)
DIALOG(R)File 144:Pascal

13056535 PASCAL No.: 97-0346520
Enteropathogens associated with diarrhea among military personnel during operation Bright Star 96, in Alexandria, Egypt
OYOFO B A; PERUSKI L F; ISMAIL T F; EL-ETR S H; CHURILLA A M; WASFY M O;

PETRUCCELLI B P; GABRIEL M E
Research Science Department, United States Naval Medical Research Unit No. 3, PSC 452, Box 5000, FPO, 09835-0007, United Arab Emirates; Walter Reed Army Institute of Research, Washington, DC 20703, United States; Uniformed Services University of the Health Sciences, Bethesda, MD 20889-5000, United States
Journal: Military medicine, 1997, 162 (6) 396-400
Language: English
This study investigated the microbial causes of diarrheal disease among U.S. troops deployed near Alexandria, Egypt, during October 1995. Bacterial causes associated with 19 cases of *diarrhea"** included: *enterotoxigenic"** Escherichia *coli"** (*ETEC"**), 42% (21% heat-stable, 11% *heat"**-*labile"**, and 11% heat-stable/ *heat"**-*labile"** producers); enteropathogenic E. coli (5.3%); and enteroadherent E. coli (42%). Four cases of diarrhea were associated with enteroaggregative E. coli based on probe analysis for enteroaggregative heat-stable enterotoxin 1. Protozoan causes included: Entamoeba histolytica (11%), E. hartmanni (5%), E. nana (5%), Blastocystis hominis (5%), Chilomastix mesnili (11%), Dientamoeba fragilis (5%), Entamoeba coli (5%), and Cryptosporidium (5%). Shigella, Aeromonas, Plesiomonas, Vibrio, Campylobacter, and Salmonella were not detected. Of the eight ETEC cases, one was *colonization"** *factor"** *antigen"** (*CFA"**)/I only, one was both *CFA"**/I and *CFA"** /III, three were *CFA"**/II, two were *CFA"**/IV, and two were *CFA"** -negative. Antibiograms of the ETEC and enteroadherent E. coli strains showed that all isolates were susceptible to norfloxacin, ciprofloxacin, and nalidixic acid but resistant to ampicillin, tetracycline, chloramphenicol, and sulfamethoxazole.

14/3,AB/13 (Item 9 from file: 144)
DIALOG(R)File 144:Pascal

13048580 PASCAL No.: 97-0338366
Analysis of incidence of infection with enterotoxigenic Escherichia coli in a prospective cohort study of infant diarrhea in Nicaragua
PANIAGUA M; ESPINOZA F; RINGMAN M; REIZENSTEIN E; SVENNERHOLM A M; HALLANDER H
Department of Microbiology, National Autonomous University (UNAN), Leon, Nicaragua; Swedish Institut for Infectious Disease Control (SMI), Stockholm , Sweden; University of Goeteborg, Goeteborg, Sweden
Journal: Journal of clinical microbiology, 1997, 35 (6) 1404-1410
Language: English
*Diarrheal"** episodes with *enterotoxigenic"** Escherichia *coli"** (*ETEC"**) were prospectively monitored during the first 2 years of life in a cohort of 235 infants from Le6n, Nicaragua. ETEC was an etiological finding in 38% (310 of 808) of diarrheal episodes and in 19% (277 of 1,472) of samples taken as asymptomatic controls at defined age intervals (P = <0.0001). The majority of diarrheal episodes (80%) occurred before 12 months of age. The major ETEC type was characterized by colonization factor *CFA"** I and elaboration of both *heat"**-*labile"** enterotoxin and heat-stable enterotoxin (ST). The proportion of E. coli strains with *CFA"** I was significantly higher in cases with diarrhea (P = 0.002). The second most prevalent type showed putative colonization factor PCFOI66 and production of ST. The prevalence of PCFO166 was approximately 20%, higher than reported before. Children with a first *CFA"** I episode contracted a

second ETEC *CFA"** I infection 24% of the time, compared with 46% for ETEC strains of any subtype. Most of the ETEC episodes were of moderate severity, and only 5% (15 of 310) were characterized as severe. In conclusion, our results give valuable information for the planning of intervention studies using ETEC vaccines.

14/3,AB/14 (Item 10 from file: 144)
DIALOG(R)File 144:Pascal

12879939 PASCAL No.: 97-0142599
Distribution of *colonization"** *factor"** *antigens"** among *enterotoxigenic"** Escherichia *coli"** strains isolated from patients with *diarrhea"** in Nepal, Indonesia, Peru, and Thailand
NIRDNOY W; SERICHANTALERGS O; CRAVIOTO A; LEBRON C; WOLF M; HOGE C W; SVENNERHOLM A M; TAYLOR D N; ECHEVERRIA P
Department of Bacteriology, Immunology, and Molecular Genetics, Armed Forces Research Institute of Medical Sciences, Bangkok, Thailand; Facultad de Medicina UNAM, Edificio B Primer Piso, Mexico City, Mexico; Naval Medical Research Unit No. 2, Jakarta, Indonesia; Walter Reed Army Institute of Research, Washington, D.C., United States; Department of Medical Microbiology & Immunology, University of Goteborg, Guldhedsgatan 10, 413-46 Goteborg, Sweden; Naval Medical Research Institute Detachment, Lima, Peru
Journal: Journal of clinical microbiology, 1997, 35 (2) 527-530
Language: English
Samples (1,318) of enterotoxigenic Escherichia coli (ETEC) isolated in 1994-1995 from children with diarrhea from Nepal, Indonesia, Peru, and Thailand were examined for *colonization"** *factor"** *antigen"** (*CFA"**) and coli surface (CS) antigens. Fifty-five percent of 361 *heat"**-*labile"** and heat-stable (*LT"**-ST), 14% of 620 *LT"**-only, and 48% of 337 ST-only ETEC had *CFA"**/CS antigens. *LT"**-ST ETEC strains were predominantly in the *CFA"** II group, and ST only strains were in the *CFA"** IV group. Additional studies are needed to identify ETEC strains that do not have *CFA"**/CS antigens.

14/3,AB/15 (Item 11 from file: 144)
DIALOG(R)File 144:Pascal

12858496 PASCAL No.: 97-0079839
A new fimbrial putative colonization factor (PCF02) in human enterotoxigenic Escherichia coli isolated in Brazil
RICCI L C; DE FARIA F P; DE S PORTO P S; DE OLIVEIRA E M G; PESTANA DE CASTRO A F
Department of Microbiology and Immunology, Institute of Biology, University of Campinas, Sao Paulo CEP: 13084-100, Brazil
Journal: Research in microbiology : (Paris), 1997, 148 (1) 65-69
Language: English Summary Language: French
Plusieurs facteurs antigeniques de colonisation (*CFA"**) et facteurs presumes de colonisation (PCF) ont ete decrits chez des souches de Escherichia coli enterotoxinogenes (ETEC). Toutefois, il existe encore de nombreuses souches d'*ETEC"**, isolees chez des patients *diarrheiques"**,

qui ne presentent aucun de ces antigenes. Etudiant 87 ETECs isolees au Bresil chez des enfants atteints de diarrhee, nous avons selectionne deux souches appartenant au type serologique O2 :H1 et qui sont capables de s'agglutiner en presence de D-mannose et de cellules sanguines humaines ou de bovins, poulets, hamsters, moutons et chevaux. L'hemaglutination resistante au D-mannose (MRHA), les reactions serologiques specifiques et les ultrastructures fimbrillaires ont pu etre observees chez les souches cultivees a 37 Degree C, mais non chez celles cultivees a 16 Degree C. L'analyse, par SDS-PAGE (sodium dodecyl sulphate/polyacrylamide gel electrophoresis), de la fraction fimbrillaire purifiee a revele une bande de 32,5 kDa. Les tests d'hybridation utilisant la sonde *LT"** (toxine thermolabile) ont identifie la codification de l'enterotoxine sur un seul plasmide a environ 34MDa. Par ailleurs, chez les souches isolees sur le critere *LT"** , le phenotype fimbrie a ete confirme. Les caracteres specifiques des fimbrilles decrites correspondent a un nouveau facteur presume de colonisation des ETECs, et le code propose est PCF02.

14/3,AB/16 (Item 12 from file: 144)
DIALOG(R)File 144:Pascal

12751651 PASCAL No.: 96-0465092
Colonization factors of enterotoxigenic Escherichia coli isolated from children in North India
SOMMERFELT H; STEINSLAND H; GREWAL H M S; VIBOUD G I; BHANDARI N; GAASTRA W; SVENNERHOLM A M; BHAN M K
Center for International Health, Haukeland Hospital, University of Bergen, Laboratory for Biotechnology, Bergen High Technology Center, University of Bergen, Bergen, Norway; Department of Microbiology and Immunology, Gade Institute, University of Bergen, Bergen, Norway; Department of Pediatrics, Division of Gastroenterology and Enteric Infections, All India Institute of Medical Sciences, New Dehli, India; Department of Medical Microbiology and Immunology, University of Goeteborg, Goeteborg, Sweden; Institute of Infectious Diseases and Immunology, Faculty of Veterinary Medicine, University of Utrecht, Utrecht, Netherlands
Journal: The Journal of infectious diseases, 1996, 174 (4) 768-776
Language: English
*Colonization"** *factor"** *antigens"** (*CFAs"**) mediate attachment of enterotoxigenic Escherichia coli (ETEC) to the intestinal mucosa and induce protective immunity against *ETEC"** *diarrhea"**. *ETEC"** strains (n = 111) isolated from North Indian children from 1985 to 1989 were examined for *CFAs"** and putative colonization factors (PCFs). *CFA"**/IV was the most common factor (26%), followed by coli surface antigen 17 (CS17) (19%), *CFA"**/I (14%), PCFO166 (7%), and *CFA"** /II (5%), while 24% of the isolates were negative for *CFAs"** and PCFs. Among the strains producing heat-stable and *heat"**-*labile"** toxin (ST SUP + *LT"** SUP + strains), the STaI gene was strongly associated with the absence of known *CFAs"** and PCFs, making the STaI SUP + *LT"** SUP + isolates an interesting target for the identification of previously undescribed factors. Repetitive sequence-based polymerase chain reaction revealed that the CS17 SUP + strains, although clonally related, represented endemically circulating strains with a diversity greater than that of the *CFA"**/I SUP + strains, which showed a substantial clonal clustering.

14/3,AB/17 (Item 13 from file: 144)
DIALOG(R)File 144:Pascal

12631373 PASCAL No.: 96-0324559
*Enterotoxigenic"** Escherichia *coli"** associated *diarrhoea"** among infants aged less than six months in Calcutta, India
GHOSH A R; KOLEY H; DE D; PAUL M; NAIR G B; SEN D
Department of Microbiology, National Institute of Cholera and Enteric Diseases, P33, Calcutta, India
Journal: European journal of epidemiology, 1996, 12 (1) 81-84
Language: English
The role of *enterotoxigenic"** Escherichia *coli"** (*ETEC"**) as etiologic agents of *diarrhoea"** in infants aged less than six months was assessed in a hospital based study in Calcutta, India. Of the 218 cases examined, ETEC strains were isolated from 26 (11.9%) cases. Among these, in 17 cases ETEC was the sole infecting pathogen (p = 0.0085), Of the 26 isolates (each isolate representing a case), 24 were distributed among seven different O :K :H serotypes and two different *colonization"** *factor"** *antigens"** (*CFAs"**) I and II. Two of the remaining isolation were untypable, non-haemagglutinating, and were non-hydrophobic as measured by the salt aggregation test (SAT). Of the 26 ETEC strains detected, 15 (57.7%) produced *heat"**-*labile"** toxin (*LT"**) only, 8 (30.8%) liberated heat-stable toxin (ST) only, and the remaining 3 (11.5%) produced both *LT"** and ST. No ETEC strain was isolated from the 102 age-matched controls included in this study. All the ETEC isolates were multiple drug resistant. The study showed that the *diarrhoea"** due to *ETEC"** was of brief duration, mostly within the range of 3 to 7 days.

14/3,AB/18 (Item 14 from file: 144)
DIALOG(R)File 144:Pascal

12524963 PASCAL No.: 96-0199413
Optimization of the intestinal lavage procedure for determination of intestinal immune responses
AHREN C; ANDERSSON K; WIKLUND G; WENNERAS C; SVENNERHOLM A M
Department of Medical Microbiology and Immunology, Goeteborg University, Goeteborg, Sweden
Journal: Vaccine, 1995, 13 (18) 1754-1758
Language: English
Optimal conditions to process, concentrate and store intestinal lavage fluid were studied in samples collected from volunteers before and after *oral"** *immunization"** with a prototype *vaccine"** against *enterotoxigenic"** Escherichia *coli"** (*ETEC"**) *diarrhoea"**. Total IgA and specific IgA antibody titres against enterotoxin and *colonization"** *factor"** *antigen"** were determined in 22 lavage samples which were either enzyme-inhibited or heat-inactivated and then subjected to different long-term storage conditions. Samples were analysed within 1 month of collection and also after 3, 6 and 24 months of storage. Total IgA concentrations and specific IgA antibody levels were higher in lavage samples treated with enzyme inhibitors (soybean trypsin inhibitor and phenylinethylsulfonyl fluoride) than in those heat-inactivated. Similarily, concentration of the lavage fluid by freeze-drying was superior to concentration against polyethylene glycol. Specific antibody titres

remained elevated after storage for at least 6 months but declined after 2 years in frozen compared with freeze-dried samples.

14/3,AB/19 (Item 15 from file: 144)
DIALOG(R)File 144:Pascal

12505177 PASCAL No.: 96-0175448
Simultaneous expression of *CFA"**/I and CS3 *colonization"** *factor"** *antigens"** of enterotoxigenic Escherichia coli by DELTA aroC, DELTA aroD Salmonella typhi *vaccine"** strain CVD 908
GIRON J A; XU J G; GONZALEZ C R; HONE D; KAPER J B; LEVINE M M
Center for Vaccine Development, Division of Geographic Medicine, School of Medicine, University of Maryland, 10 South Pine St., Baltimore, MD 21201, USA
Journal: Vaccine, 1995, 13 (10) 939-946
Language: English
Among the known colonization factors of enterotoxigenic Escherichia coli (ETEC), *CFA"**/I and CS3 (the common antigen in the *CFA"**/II family of fimbrial antigens) are two of the most prevalent fimbrial antigens found in clinical isolates but are never expressed by the same wild-type strain. We manipulated the genetic determinants encoding CS3 and *CFA"**/I fimbriae so that these two important colonization factors are expressed simultaneously in attenuated Salmonella typhi live *oral"** *vaccine"** strain CVD 908, including after growth in liquid medium (*CFA"**/I is poorly expressed by wild-type ETEC in broth culture). The recombinant fimbrial structures produced by CVD 908 are morphologically indistinguishablefrom the CS3 fibrillae and *CFA"** /1 rod-like fiInbriae produced by ETEC, and are recognized by monospecific CS3 and *CFA"**/1 antibodies. This prototype construct may prove useful in investigating the live vector approach to immunoprophylaxis of *ETEC"** *diarrheal"** disease.

14/3,AB/20 (Item 16 from file: 144)
DIALOG(R)File 144:Pascal

12461030 PASCAL No.: 96-0122990
Colonisation factors amongst clinical isolates of enterotoxigenic Escherichia coli
IYER L; VADIVELU J; PARASAKTHI N
Univ. Malaya, fac. medicine, dep. medical microbiology, 59100 Kuala Lumpur, Malaysia
Journal: Singapore medical journal, 1995, 36 (5) 495-497
Language: English
The production of *heat"**-*labile"** (*LT"**) and heat-stable (ST) enterotoxins, *colonisation"** *factor"** *antigens"** (*CFAs"**) and haemagglutinins was investigated amongst 310 Escherichia coli (E. coli) isolates obtained from 62 children under the age of five, with diarrhoea. Twenty-one isolates were found to produce enterotoxins, of which fifteen (71%) isolates produced ST only, 2 (10%) produced *LT"** only and 4 (19%) produced both *LT"** and ST. However, none of the isolates demonstrated any of the common *CFAs"** identified to date, but 8 out of the 21 isolates demonstrated haemagglutination with rabbit, sheep or human group A erythrocytes, suggesting the presence of putative *CFAs"** , yet unidentified.

14/3,AB/21 (Item 17 from file: 144)
DIALOG(R)File 144:Pascal

12255247 PASCAL No.: 95-0480760
A survey of enteropathogens among United States military personnel during operation bright Star '94, in Cairo, Egypt
OYOFO B A; EL-GENDY A; WASFY M O; EL-ETR S H; CHURILLA A; MURPHY J
U.S. Naval medical res. unit, enteric microbiology branch, FPO AE 09835-0007, USA
Journal: Military medicine, 1995, 160 (7) 331-334
Language: English
Acute gastroenteritis is a potential cause of substantial morbidity in U.S. military personnel during deployment. This study was conducted to evaluate enteric pathogens associated with diarrhea in a U.S. military population on deployment in Cairo, Egypt, during November 1993. Enteric pathogens found to be associated with cases of *diarrhea"** included: *enterotoxigenic"** Escherichia *coli"** (*ETEC"**), 27% (22% heat-stable (ST), 3% *heat"**-*labile"** (*LT"**), and 2% STILT producers); Campylobacter spp., 3%; and Salmonella spp. 3%. Other enteric pathogens, namely Shigella, Aeromonas, Plesiomonas, Vibrio spp., Bacillus cereus, and enteric parasites, were not found in any of the 36 patients. Of the 8 patients who were ETEC-positive, three expressed *colonization"** *factor"** *antigens"** (*CFA"**)/II, and two expressed putative *colonization"** *factor"** *antigen"** (PCF) 0159. All of the latter isolates produced ST. ETEC with different surface protein antigens were found to have surface hydrophobicity in the range of 0.2 M to greater than 2.0 M. Plasmid profiles of the ETEC strains showed no correlation with toxin production. In vitro susceptibility testing of the ETEC strain showed that 32% of the strains were resistant to three or more antimicrobial agents, whereas 24% showed 100% susceptibility. The enteropathogens tested were susceptible to norfloxacin, ciprofloxacin, and nalidixic acid, suggesting that the quinolones might be useful for the treatment of diarrheic patients.

14/3,AB/22 (Item 18 from file: 144)
DIALOG(R)File 144:Pascal

11375697 PASCAL No.: 94-0202466
A new fimbrial putative colonization factor, PCF020, in human enterotoxigenic Escherichia coli
VIBOUD G I; BINSZTEIN N; SVENNERHOLM A M
Univ. Goeteborg, dep. medical microbiology immunology, 41346 Goeteborg, Sweden
Journal: Infection and immunity, 1993, 61 (12) 5190-5197
Language: English
The ability to colonize the small intestine is essential for *enterotoxigenic"** Escherichia *coli"** (*ETEC"**) to cause *diarrhea"**. Several *colonization"** *factor"** *antigens"** (*CFAs"**) and putative colonization factors (PCFs) have been described for ETEC. However, there are still many *ETEC"** strains isolated from patients with *diarrhea"** which do not possess any of these antigens. To identify *CFAs"** in ETEC lacing the above-mentioned antigens, we exploited the ability of ETEC to adhere to tissue-cultured cells from an enterocyte-like cell line, Caco-2. An ETEC strain producing *heat"**-*labile"** toxin and heat-stable toxin of

serotype 020:K27:H- (ARG-2) that was isolated from a child with diarrhea in Argentina and bound to Caco-2 cells was studied in further detail

14/3,AB/23 (Item 19 from file: 144)
DIALOG(R)File 144:Pascal

11257030 PASCAL No.: 94-0075567
Serotypes and colonization factors of enterotoxigenic Escherichia coli isolated in various countries
BLANCO J; BLANCO M; GONZALEZ E A; BLANCO J E; ALONSO M P; GARABAL J I; JANSEN W H
Univ. Santiago, fac. veterinaria, dep. microbioloxia parasitoloxia, 27002 Lugo, Spain
Journal: European journal of epidemiology, 1993, 9 (5) 489-496
Language: English
One hundred and six enterotoxigenic E. coli (ETEC) isolated from many geographical areas were serotyped and investigated for the presence of *colonization"** *factor"** *antigens"** *CFA"**/I and *CFA"**/II, the expression of mannose-resistant haemagglutination (MRHA) and the levels of surface hydrophobicity. *CFA"**/I was found in 6 (17%) of 16 *LT"** SUP + STa SUP + strains and in 15 (54%) of 28 STa SUP + strains; *CFA"**/II was found in 16 (44%) of 16 *LT"** SUP + STa SUP + strains. None of 42 *LT"** SUP + strains showed *CFA"**/I or *CFA"**/II. *CFA"**/I was found in ETEC of serotypes O61:K-:H-, O78:K80, O128:K67 and O153:K-:H45, whereas *CFA"**/II was found in serotypes O6:H-, O6:K15:H16 and O6:K?:H40

14/3,AB/24 (Item 20 from file: 144)
DIALOG(R)File 144:Pascal

11114907 PASCAL No.: 93-0621931
Intestinal antibody response after *oral"** *immunization"** with a prototype cholera B subunit-*colonization"** *factor"** *antigen"** enterotoxigenic Escherichia coli *vaccine"**
AHREN C; WENNERAS C; HOLMGREN J; SVENNERHOLM A M
Univ. Goeteborg, dep. medical microbiology immunology, 413 46 Goeteborg, Sweden
Journal: Vaccine, 1993, 11 (9) 929-934
Language: English
A prototype *oral"** enterotoxigenic Escherichia coli (ETEC) *vaccine"** containing formalin-inactivated whole bacteria expressing *colonization"** *factor"** *antigens"** *CFA"**/I and *CFA"**/II and cholera B subunit (CTB) has been tested for safety and immunogenicity in 70 adult Swedish volunteers. When given in three doses with 7-week intervals the *vaccine"** was found to be safe and to give rise to specific IgA antibody responses in intestinal lavage fluid in most of the volunteers (*CFA"**/I 82%, *CFA"**/II 82% and CTB 91%). The frequencies and magnitudes of these responses, which were already maximal after two doses, were comparable with those previously found in patients convalescing from severe *ETEC"** *diarrhoea"**

14/3,AB/25 (Item 21 from file: 144)
DIALOG(R)File 144:Pascal

10964924 PASCAL No.: 93-0474390
Loss of some virulence factors of enterotoxigenic Escherichia coli on repeated subcultures
SHOBHA RAM; KHURANA S; SINGH R P; KHURANA S B
Dayanand medical coll. & hosp., dep. microbiology, Ludhiana 141005, India
Journal: Indian journal of medical research. Section A, Infectious diseases, 1992, 95 (NOV) 284-287
Language: English
Thirty enterotoxigenic Esch. coli (ETEC) strains of predominant serogroups, isolated from patients with diarrhoea in Ludhiana, Punjab were investigated for expression of *heat"** *labile"** (*LT"**) enterotoxin and *colonization"** *factor"** *antigens"** (*CFAs"**) on repeated subculture. These belonged to serogroup 078 (10), 080 (2), 0114 (6), 020 (3), 0128 (3), 0153 (2) and 08 (4) respectively. The isolates exhibited a differential response for expression of *LT"** and *CFAs"** on repeated subculturing. All the strains were positive for both *LT"** and *CFA"** up to six subcultures. Three strains of serogroup 0114 and one of 080 failed to express *CFA"** while one strain each of serogroups 080, 0114, 020 and 08 failed to elaborate *LT"** in the 8th subculture

14/3,AB/26 (Item 22 from file: 144)
DIALOG(R)File 144:Pascal

10640573 PASCAL No.: 93-0149851
Occurrence of *colonization"** *factor"** *antigens"** I & II in *enterotoxigenic"** Escherichia *coli"** associated *diarrhoea"** in Iran & correlation with severity of disease
KATOULI M; SHOKOUHI F; FARHOUDI-MOGHADDAM A A; AMINI S
Pasteur inst. Iran, microbiology dep., Tehran, Iran
Journal: Indian journal of medical research. Section A, Infectious diseases, 1992, 95 (MAI) 115-120
Language: English
The occurence of *colonization"** *factor"** *antigens"** I and II (*CFA"** /I and II) and type 1 somatic pili was investigated in 197 enterotoxigenic Esch. coli (*ETEC"**) isolated from 1967 patients of *diarrhoea"** (aged under 3 yr) during February 1985 to March 1986 in Tehran, Iran. Among ETEC strains, 154 strains were heat-stable enterotoxin (ST) producers, 27 strains were *heat"**-*labile"** enterotoxin (*LT"**) producers, and 16 strains produced both toxins

14/3,AB/27 (Item 23 from file: 144)
DIALOG(R)File 144:Pascal

10248395 PASCAL No.: 92-0454303
*Oral"** ingestion of egg yolk immunoglobulin from hens *immunized"** with an *enterotoxigenic"** Escherichia *coli"** strain prevents *diarrhea"** in rabbits challenged with the same strain
O'FARRELLY C; BRANTON D; WANKE C A
Harvard univ., biological laboratories, Cambridge MA 02138, USA
Journal: Infection and immunity, 1992, 60 (7) 2593-2597
Language: English
White Leghorn hens were *immunized"** with enterotoxigenic Escherichia coli B16-4 with *heat"**-*labile"** enterotoxin and *colonization"**

*factor"** *antigen"** I in Freund's adjuvant. Specific antibodies were detected by an enzyme-linked immunosorbent assay in the serum after 8 days and in eggs after 10 days, with levels reaching peaks at 15 and 20 days after the first *immunization"**, respectively. The protective effects of the egg yolk antibodies were tested in the rabbit reversible ileal tie model of diarrhea. Five control rabbits developed severe diarrhea within 72 h after inoculation with enterotoxigenic E. coli B16-4

14/3,AB/28 (Item 24 from file: 144)
DIALOG(R)File 144:Pascal

08626539 PASCAL No.: 89-0175700
Non-replicating *oral"** whole cell *vaccine"** protective against *enterotoxigenic"** Escherichia *coli"** (*ETEC"**) *diarrhea"**: stimulation of anti-*CFA"** (*CFA"**/I) and anti-enterotoxin (anti-*LT"**) intestinal IgA and protection against challenge with ETEC belonging to heterologous serotypes
EVANS D G; EVANS D J JR; OPEKUN A R; GRAHAM D Y
Veterans administration medical cent., Houston TX 77211, USA
Journal: FEMS microbiology letters, 1988, 47 (3) 117-125
Language: English

14/3,AB/29 (Item 25 from file: 144)
DIALOG(R)File 144:Pascal

05427356 PASCAL No.: 85-0199721
Administration of purified *colonization"** *factor"** *antigen"** (*CFA"**/I, *CFA"**/II) of enterotoxigenic Escherichia coli to volunteers: response to challenge with virulent enterotoxigenic Escherichia coli
EVANS D G; GRAHAM D Y; EVANS D J JR; OPEKUN A
VA medical center, Houston TX 77211, USA
Journal: Gastroenterology, 1984, 87 (4) 934-940
Language: English
Le developpement d'un *vaccin"** contre la *diarrhee"** a l'*enterotoxine"** d'E. *Coli"** utilisant des antigenes de facteur de colonisation purifies pour induire une reponse d'IgA elevee a ces antigenes proteiques solubles necessite une evaluation systematique des regimes d'*immunisation"** pour decouvrir la combinaison optimale de la forme d'antigene, la dose, la voie d'administration

14/3,AB/30 (Item 1 from file: 266)
DIALOG(R)File 266:FEDRIP

00329121
IDENTIFYING NO.: 1Z01HD02500-09 AGENCY CODE: CRISP
ETEC Epidemiology and *Vaccine"** Research in Lower Egypt
PRINCIPAL INVESTIGATOR: RAO, MALLA R
ADDRESS: NICHD, NIH
SPONSORING ORG.: NATIONAL INSTITUTE OF CHILD HEALTH AND HUMAN DEVELOPMENT
FY : 2001
SUMMARY: *Enterotoxigenic"** Escherichia *coli"** (*ETEC"**) *diarrhea"** is hyperendemic among young Egy ptian children, with a balanced

distribution of toxin phenotypes from pathogenic isolates. These features make it logical to develop a field site for the evalua tion of ETEC epidemiology and ETEC *vaccines"** in Egypt. We have been engaged in a collaborative program of research in lower Egypt designed to characterize ETEC d iarrhea in a pediatric cohort and to test the safety and immunogenicity of a pro mising killed *oral"** ETEC *vaccine"** candidate in preparation for a field trial of va ccine efficacy,which commenced in January 1999. We have followed a cohort of 397 children under 3 years with twice-weekly active surveillance in Abu Homos (Behe ira governorate) to determine the age-specific incidence rate of *ETEC"** *diarrhea"**, by toxin and colonization factor (*CFA"**) phenotypes. During 30 months of follow-up of the children, *ETEC"** was isolated in 25% of *diarrheal"** episodes; the incidence rates of *ETEC"** (episodes per child-year) were 1.7, 1.6, and 0.7 in the first, sec ond, and third years of life. Concurrent with establishment of this surveillance , we conducted randomized, placebo-controlled Phase 2 studies of killed *oral"** ETE C *vaccine"** , administered as a two-dose regimen to 76 adults, 107 children aged 6- 12 years, 106 children aged 2-5 years, and 95 children aged 6-18 months in Benha , near Cairo. Each of these studies demonstrated the *vaccine"** to be well-tolerate d and to induce significant mucosal immune responses to *vaccine"** antigens. In Jan uary 1999, a Phase III trial of the *vaccine"** that will assess the safety, immunog enicity, and clinical efficacy of the *vaccine"**, was initiated in Abu Homos. 192 c hildren 6-18 months of age were randomized to receive either *vaccine"** or placebo, and surveillance for potential adverse effects and diarrheal outcomes continues . In January 2000, an additional 161 children were randomized to receive either *vaccine"** or placebo, and they also remain under surveillance. In June 2000, a Pha se II trial of the ETEC *vaccine"** was initiated to evaluate its safety and immunog enicity when administered in conjunction with the expanded program on *immunizati"** on (EPI) *vaccines"** viz. DTP, Polio and Hepatitis B *vaccines"**.

14/3,AB/31 (Item 1 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)

12911745 References: 47
TITLE: Construction and characterization of genetically defined aro omp mutants of enterotoxigenic Escherichia coli and preliminary studies of safety and immunogenicity in humans
AUTHOR(S): Turner AK; Terry TD; Sack DA; Londono-Arcila P; Darsley MJ (REPRINT)
AUTHOR(S) E-MAIL: michael.darsley@acambis.co.uk
CORPORATE SOURCE: Acambis Ltd, Peterhouse Technol Pk,100 Fulbourn Rd/Cambridge CB1 9PT//England/ (REPRINT); Acambis Ltd, /Cambridge CB1 9PT//England/; Johns Hopkins Univ, Vaccine Testing Unit, /Baltimore//MD/
PUBLICATION TYPE: JOURNAL
PUBLICATION: INFECTION AND IMMUNITY, 2001, V69, N8 (AUG), P4969-4979
GENUINE ARTICLE#: 456UP
PUBLISHER: AMER SOC MICROBIOLOGY, 1752 N ST NW, WASHINGTON, DC 20036-2904 USA
ISSN: 0019-9567
LANGUAGE: English DOCUMENT TYPE: ARTICLE

ABSTRACT: Enterotoxigenic Escherichia coli (*ETEC"**) is a leading cause of *diarrhea"** in travelers to countries where the disease is endemic and causes a major disease burden in the indigenous population, particularly

children. We describe here the generation and preclinical characterization of candidate strains of ETEC which are intended to provide the basis of a live attenuated *oral"** *vaccine"** to prevent this disease. It has been shown previously that a spontaneously arising toxin-negative variant ETEC strain, E1392/75-2A, could confer 75% protection against challenge when administered to volunteers. Unfortunately this strain induced mild diarrhea in 15% of recipients. To eliminate the unacceptable reactogenicity of strain E1392/75-2A, it was further attenuated by introducing three different combinations of defined deletion mutations into the chromosome. A mouse intranasal model of *immunization"** was developed and used to show that all of the strains were immunogenic. Immune responses against *colonization"** *factor"** *antigens"** (*CFAs"**) were particularly strong when the bacterial inocula were grown on "*CFA"** agar," which induces strong expression of these antigens. Two of the strains were selected for a phase I dose escalation safety study with healthy adult volunteers. Freshly grown organisms were harvested from *CFA"** agar plates and administered to volunteers as a suspension containing from 5 x 10(7) to 5 x 10(9) CFU. The *vaccine"** was well tolerated at all doses and induced significant immune responses in all recipients at the highest dose of either strain. The results provide the basis for further clinical evaluation of these *vaccine"** candidates.

14/3,AB/32 (Item 2 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)

10237173 References: 36
TITLE: Epidemiology of *enterotoxigenic"** Escherichia *coli"** *diarrhea"** in a pediatric cohort in a periurban area of lower Egypt
AUTHOR(S): Abu-Elyazeed R (REPRINT); Wierzba TF; Mourad AS; Peruski LE; Kay BA; Rao M; Churilla AM; Bourgeois AL; Mortagy AK; Kamal SM; Savarino SJ; Campbell JR; Murphy JR; Naficy A; Clemens JD
CORPORATE SOURCE: USN, Med Res Unit 3, Attn Code 101F,PSC 452,Box 5000/FPO//AE/09835 (REPRINT); USN, Med Res Unit 3, /Cairo//Egypt/; NICHHD, NIH, /Bethesda//MD/20892; Natl Naval Med Res Inst, /Bethesda//MD/20814
PUBLICATION TYPE: JOURNAL
PUBLICATION: JOURNAL OF INFECTIOUS DISEASES, 1999, V179, N2 (FEB), P382-389
GENUINE ARTICLE#: 162QB
PUBLISHER: UNIV CHICAGO PRESS, 5801 S ELLIS AVENUE, CHICAGO, IL 60637 USA
ISSN: 0022-1899
LANGUAGE: English DOCUMENT TYPE: ARTICLE

ABSTRACT: Enterotoxigenic Escherichia coil (ETEC) are diverse pathogens that express *heat"**-*labile"** (*LT"**) and/or heat-stable (ST) enterotoxins, yet little is known about whether epidemiologic patterns of pediatric *ETEC"** *diarrhea"** vary by the expressed *ETEC"** toxin phenotype, In total, 242 Egyptian children aged <3 years were prospectively followed in 1993-1995. ETEC episodes were detected during twice-weekly home visits, and asymptomatic ETEC excretion was identified from monthly cross-sectional surveys. ETEC episodes were 0.6 per child-year. ST-only ETEC was 2.6 times (P < .001) more common in warmer than cooler months, while *LT"**-only ETEC showed no seasonal variation. Ownership of a household sanitary latrine, but not breast-feeding, was associated with a lower risk of both enterotoxin phenotypes, Coexpression of a colonization factor by *LT"**- or ST-only *ETEC"** strengthened the association with *diarrhea"**, These findings indicate that the epidemiologic patterns of

*LT"**-only and ST-only ETEC are not identical and that disease interventions should include improved household sanitation.

14/3,AB/33 (Item 3 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)

07021585 References: 33
TITLE: COLONIZATION FACTORS OF ENTEROTOXIGENIC E-COLI (ETEC) FROM RESIDENTS OF NORTHERN EGYPT
AUTHOR(S): OYOFO BA; ELETR SH; WASFY MO; PERUSKI L; KAY B; MANSOUR M; CAMPBELL JR; SVENNERHOLM AM; CHURILLA AM; MURPHY JR
CORPORATE SOURCE: USN,MED RES UNIT 3,RES PUBLICAT BRANCH,PSC 452,BOX 5000/FPO//AE/09835 (Reprint); USN,MED RES UNIT 3/CAIRO//EGYPT/
PUBLICATION: MICROBIOLOGICAL RESEARCH, 1995, V150, N4 (NOV), P429-436
GENUINE ARTICLE#: TN149
ISSN: 0944-5013
LANGUAGE: ENGLISH DOCUMENT TYPE: ARTICLE

ABSTRACT: Infection caused by enterotoxigenic Escherichia coli (ETEC) poses a serious health problem to children in developing countries. Colonization of the small intestinal mucosa by ETEC strains is mediated by antigenically specific fimbriae, also known as *colonization"** *factor"** *antigens"** (*CFA"**). The importance of this study arises from reports that active and passive immunization with ETEC strains harboring *CFAs"** induced protective immunity against diarrhea in animal models with preformed antibodies. In humans, ETEC containing *CFA"**/I, II, III and IV have been identified. The aim of this study was to define *CFAs"** of ETEC isolated in Alexandria, Egypt. One hundred and seven ETEC isolates from 132 human residents in Alexandria, Egypt were isolated during a birth cohort study. ETEC isolates were screened for *heat"** *labile"** (*LT"**) and heat stable (ST) toxins using a P-32 oligonucleotide hybridization probe and a GM1 ELISA. These isolates were examined using monoclonal antibodies against CPA/I, II, III, IV, and against the putative colonization antigens PCF0159 and PCF0166, CS 7 and CS 17. *CFAs"** were found in 48% of ETEC strains. *CFA"**/I was found in 18% of the strains, *CFA"**/II in 10% and *CFA"**/IV in 14%. *CFA"** III was not found. All fifteen strains expressing *CFA"** /IV expressed CS6 and produced ST. *CFA"**/IV was not found in non-ST producing strains, while *CFA"**/I was absent in ST - only producing strains.

14/3,AB/34 (Item 4 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)

05191089 References: 41
TITLE: MOLECULAR CHARACTERIZATION OF ENTEROTOXIGENIC ESCHERICHIA COLI (ETEC) ISOLATED IN NEW CALEDONIA (VALUE OF POTENTIAL PROTECTIVE ANTIGENS IN *ORAL"** *VACCINE"** CANDIDATES)
AUTHOR(S): BEGAUD E; MONDET D; GERMANI Y (Reprint)
CORPORATE SOURCE: INST PASTEUR NOUVELLE CALEDONIE,ENTER PATHOGENSLAB,BP 61/NOUMEA//NEW CALEDONIA/ (Reprint); INST PASTEUR NOUVELLE CALEDONIE,ENTER PATHOGENSLAB/NOUMEA//NEW CALEDONIA/
PUBLICATION: RESEARCH IN MICROBIOLOGY, 1993, V144, N9 (NOV-DEC), P721-728
GENUINE ARTICLE#: MU276
ISSN: 0923-2508

LANGUAGE: ENGLISH DOCUMENT TYPE: ARTICLE

ABSTRACT: The role of *enterotoxigenic"** Escherichia *coli"** (*ETEC"**) in childhood *diarrhoea"** in New Caledonia was demonstrated in previous epidemiological works. This study was undertaken in order to characterize these strains and to determine whether bacterial components of current *vaccine"** candidates (toxin. *colonization"** *factor"** *antigens"**, O:H antigens) would be useful in our region. A total of 24 ETEC strains were studied: 5 strains produced *heat"**-*labile"** enterotoxin. 17 strains produced heat-stable enterotoxin (9 STp and 8 STh), and 2 strains produced both toxins (1 *LT"**/STp/STh and 1 *LT"**/STh). E. coli strains were screened for the presence of genes encoding for enterotoxins (DNA dot blot and Southern hybridization assays); results obtained with probes were closely correlated and were in agreement with biological assays. No two ETEC strains possessed similar plasmid profiles, and DNA sequences encoding for enterotoxins were located on plasmids ranging from 58 to 75 MDa. The O:H (01:H-,02:H7, 06:H16, 025:H-, 027:H7, 028ab:H9, 052:H10, 064:H5, 070:H-, 078:H12, 088:H25, 099:H6, 0101:H-, 0126:H12, 0166:H30) serotypes are presented (all the strains were typable, but some ETEC serotypes were unusual). By using antisera against *colonization"** *factor"** *antigens"** (*CFA"**) I and It, results showed that 9 of the 24 ETEC strains expressed *CFA"** (2 *CFA"**/II and 7 *CFA"**/I). These strains possessed high bacterial surface hydrophobicity. Fifteen ETEC did not possess *CFA"**; among these, 11 did not exhibit high hydrophobicity or show haemagglutination activity. Four of the 15 *CFA"**-negative strains exhibited high hydrophobicity (two 064:H45. one 070:H- and one 088:H25) but no haemagglutination in the presence or absence of mannose. Only 7 of 24 ETEC expressed resistance to ampicillin, trimethoprimsulphamethoxazole or tetracycline. Data indicate that several ETEC isolates would be refractory to current *Vaccine"** candidates, and that for *vaccine"** to be effective in our region, other antigens must be included.

14/3,AB/35 (Item 5 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)

05036486 References: 32
TITLE: A NEW FIMBRIAL PUTATIVE COLONIZATION FACTOR, PCFO20, IN HUMAN ENTEROTOXIGENIC ESCHERICHIA COLI
AUTHOR(S): VIBOUD GI; BINSZTEIN N; SVENNERHOLM AM (Reprint)
CORPORATE SOURCE: UNIV GOTEBORG,DEPT MED MICROBIOL & IMMUNOL,GULDHEDSGATAN 10/S-41346 GOTHENBURG//SWEDEN/ (Reprint); UNIV GOTEBORG,DEPT MED MICROBIOL & IMMUNOL/S-41346 GOTHENBURG//SWEDEN/; INST NACL MICROBIOL,DIV PHYSIOPATHOGENESIS/RA-1281 BUENOS AIRES/DF/ARGENTINA/
PUBLICATION: INFECTION AND IMMUNITY, 1993, V61, N12 (DEC), P5190-5197
GENUINE ARTICLE#: MH823
ISSN: 0019-9567
LANGUAGE: ENGLISH DOCUMENT TYPE: ARTICLE

ABSTRACT: The ability to colonize the small intestine is essential for *enterotoxigenic"** Escherichia *coli"** (*ETEC"**) to cause *diarrhea"**. Several *colonization"** *factor"** *antigens"** (*CFAs"**) and putative colonization factors (PCFs) have been described for ETEC. However, there are still many *ETEC"** strains isolated from patients with *diarrhea"** which do not possess any of these antigens. To identify *CFAs"** in ETEC lacking the above-mentioned antigens, we exploited the ability of ETEC to adhere to tissue-cultured cells from an enterocyte-like cell line, Caco-2.

An ETEC strain producing *heat"**-*labile"** toxin and heat-stable toxin of serotype O20:K27:H- (ARG-2) that was isolated from a child with diarrhea in Argentina and bound to Caco-2 cells was studied in further detail. Sodium dodecyl sulfate-polyacrylamide gel electrophoresis (SDS-PAGE) analyses of this strain revealed a band of 25 kDa when bacteria were grown at 37 degrees C that was missing when the same strain was cultured at 20 degrees C. Furthermore, electron microscopy examination revealed the presence of fimbriae on the surfaces of cells of this strain when cells were grown at 37 degrees C but not at 20 degrees C. Rabbit antiserum raised against purified fimbriae reacted with the 25-kDa protein in immunoblotting and bound specifically to the fimbriae, as shown by immunoelectron microscopy. The presence of fimbriae, adhesion to Caco-2 cells, and the 25-kDa band seen in the SDS-PAGE were all simultaneously lost by single-insertion mutations. The N-terminal amino acid sequence of the protein subunit of the fimbriae showed no relation with those of the known colonization factors of ETEC. Furthermore, the fimbriae of the ARG-2 strain did not cross-react immunologically with any of the previously described adhesive factors in human ETEC when specific antisera against *colonization"** *factor"** *antigens"** and putative colonization factors were used. Moreover, a specific antiserum raised against the fimbriae in ARG-2 did not react with ETEC carrying known colonization factors. We propose to name these new fimbriae PCFO20.

14/3,AB/36 (Item 6 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)

04363226 References: 36
TITLE: CHARACTERIZATION OF MONOCLONAL ANTIBODIES AGAINST PUTATIVE COLONIZATION FACTORS OF ENTEROTOXIGENIC ESCHERICHIA-COLI AND THEIR USE IN AN EPIDEMIOLOGICAL STUDY
AUTHOR(S): VIBOUD GI; BINSZTEIN N; SVENNERHOLM AM (Reprint)
CORPORATE SOURCE: GOTHENBURG UNIV,DEPT MED MICROBIOL & IMMUNOL/S-41346 GOTHENBURG//SWEDEN/ (Reprint); GOTHENBURG UNIV,DEPT MED MICROBIOL & IMMUNOL/S-41346 GOTHENBURG//SWEDEN/; INST NACL MICROBIOL CARLOS G MALBRAN/RA-1281 BUENOS AIRES/DF/ARGENTINA/
PUBLICATION: JOURNAL OF CLINICAL MICROBIOLOGY, 1993, V31, N3 (MAR), P 558-564
GENUINE ARTICLE#: KM810
ISSN: 0095-1137
LANGUAGE: ENGLISH DOCUMENT TYPE: ARTICLE

ABSTRACT: Monoclonal antibodies (MAbs) against five putative colonization factors (PCFs), i.e., *colonization"** *factor"** *antigen"** (*CFA"**)/III, coli surface antigen (CS)7 and CS17, PCFO159, and PCFO166 of enterotoxigenic Escherichia coli (ETEC), were produced. Hybridomas (one each) producing specific antibodies against the respective PCFs were selected. All the MAbs reacted with the corresponding fimbriae but not with *CFA"**/I, *CFA"**/II, or *CFA"**/IV or the heterologous PCFs in bacterial agglutination and enzyme-linked immunosorbent assays (ELISAs). In immunoelectron microscopy these MAbs bound along the fimbriae, and they also reacted with the corresponding subunits in immunoblots. The five MAbs were used to evaluate the prevalence of *CFA"**/III, CS7, CS17, PCFO159, and PCFO166 in *ETEC"** strains isolated from children with *diarrhea"** in Argentina. One hundred five *ETEC"** isolates negative for *CFA"**/I, *CFA"**/II, and *CFA"**/IV were tested in slide agglutination or in a dot blot test for spontaneously agglutinating strains; positive results were

confirmed by inhibition ELISAs. It was found that 27% of the *CFA"** -negative ETEC strains carried one of the PCFs. The sensitivity of slide agglutination with these MAbs was similar to that with specific polyclonal antisera; however, the specificity was higher. PCFO166 was found in 9.5% of the strains tested, mainly in ETEC of serogroup 078 producing heat-stable toxin alone. CS17 and CS7 were identified in 6.7 and 5.7%, respectively, of strains producing *heat"**-*labile"** toxin only, most of which belonged to serogroup 0114. PCFO159 was found in 3.8% of the isolates tested, whereas *CFA"**/III was detected in only one ETEC strain.

14/3,AB/37 (Item 7 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)

03929429 References: 0
(NO REFS KEYED)
TITLE: *ENTEROTOXIGENIC"** AND NECROTIZING ESCHERICHIA-*COLI"** IN HUMAN *DIARRHOEA"** IN SPAIN
AUTHOR(S): BLANCO J; GONZALEZ EA; ESPINOSA P; BLANCO M; GARABAL JI; ALONSO MP
CORPORATE SOURCE: UNIV SANTIAGO,FAC VET,DEPT MICROBIOL & PARASITOL/LUGO//SPAIN/ (Reprint)
PUBLICATION: EUROPEAN JOURNAL OF EPIDEMIOLOGY, 1992, V8, N4 (JUL), P548-552
GENUINE ARTICLE#: JK282
ISSN: 0393-2990
LANGUAGE: ENGLISH DOCUMENT TYPE: ARTICLE

ABSTRACT: Enterotoxigenic Escherichia coli (ETEC) strains of serotype 0153: K-:H45 *CFA"**/I+ STa+ were associated with two outbreaks of neonatal diarrhoea that occurred in two different hospitals of Madrid, in one of which several children died. Two other outbreaks were associated with ETEC strains of serotypes 0159: K-: H21 (*LT"**+) and 0159: K-: H4 (*LT"**+ STa+) without *CFA"**/I and *CFA"**/II colonization factors. Necrotizing E. coli (NTEC) strains of serotype 06: K13, producing the cytotoxic necrotizing factor CNF1 and alpha-haemolysin, were also associated with two outbreaks of neonatal diarrhoea that occured in a hospital in Madrid and in a hospital in Talavera de la Reina. The results of the characterization of some ETEC and NTEC strains isolated from sporadic cases of diarrhoea are also discussed.

14/3,AB/38 (Item 8 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)

03832024 References: 25
TITLE: RELATIONSHIP BETWEEN *ENTEROTOXIGENIC"** ESCHERICHIA-*COLI"** AND *DIARRHEA"** AMONG CHILDREN IN BUENOS-AIRES
AUTHOR(S): BINSZTEIN N; RIVAS M; MORAL LL; VIBOUD G; IRIARTE C; SZEFNER M; SVENNERHOLM AM
CORPORATE SOURCE: INST NACL MICROBIOL CARLES G MALBRAN,DIV INMUNOL APLICADA,AVE VELEZ SARSFIELD 563/RA-1281 BUENOS AIRES//ARGENTINA/ (Reprint); HOSP PEDRO ELIZALDE/BUENOS AIRES//ARGENTINA/; GOTHENBURG UNIV,DEPT MED MICROBIOL/S-41124 GOTHENBURG//SWEDEN/
PUBLICATION: MEDICINA-BUENOS AIRES, 1992, V52, N2, P103-108
GENUINE ARTICLE#: JD611
LANGUAGE: ENGLISH DOCUMENT TYPE: ARTICLE

ABSTRACT: The incidence of enterotoxigenic Escherichia coli (ETEC) has been studied in 85 children with acute diarrhea in patients in the Hospital de Ninos Pedro de Elizalde, Buenos Aires, and in 38 healthy children. All of them were up to four years old and none had received antibiotic treatment within 7 days before sampling. ETEC was recovered in 9 out of 85 (10.6%) children with diarrhea. From these positive cases, 6 were associated with heat-stable (ST), 1 with *heat"**-*labile"** (*LT"**) and 2 with both *LT"** and ST enterotoxins. Only one case (2.6%) of *LT"**-producing ETEC was detected in the control group. In 5 out of 9 *ETEC"** *diarrhea"** cases (55.5%) the isolated strains expressed human *colonization"** *factor"** *antigens"** (*CFA"**); four of them were *CFA"**/I and one *CFA"**/II. The characteristics of the *CFA"**, biotype, serotype and antibiotic sensitivity pattern were studied in 23 E. coli isolates from 10 ETEC positive children. Of the 12 ST only strains, 5 (41.7%) expressed *CFA"**/I and 2 (16.7%) *CFA"**/II (CS2 + CS3). One out of 2 *LT"**/ST strains expressed *CFA"**/I. *CFAs"** were not detected in the ETEC-*LT"** nor in the toxin negative E coli strains. From the ETEC isolated, 82.4% were resistant to 4 or more antibiotics, whereas only 50% of simultaneously isolated toxin-negative E. coli presented this sensitivity pattern. The different ETEC strains belonged to several different serotypes, some of them rarely observed in other countries. None of these serotypes correlated either with the toxin profile or with the sugar fermentation pattern. Interestingly, in three cases, ETEC strains with differing serotype but with the same toxin profile were detected.

14/3,AB/39 (Item 9 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)

03736904 References: 26
TITLE: OCCURRENCE OF *COLONIZATION"** *FACTOR"** *ANTIGEN"**-I AND ANTIGEN-II IN *ENTEROTOXIGENIC"** ESCHERICHIA-*COLI"** ASSOCIATED *DIARRHOEA"** IN IRAN AND CORRELATION WITH SEVERITY OF DISEASE
AUTHOR(S): KATOULI M; SHOKOUHI F; FARHOUDIMOGHADDAM AA; AMINI S
CORPORATE SOURCE: KAROLINSKA INST,DEPT BACTERIOL,BOX 60400/S-10401 STOCKHOLM 60//SWEDEN/ (Reprint); PASTEUR INST IRAN,DEPT MICROBIOL/TEHRAN//IRAN/; PASTEUR INST IRAN,DEPT VIROL/TEHRAN//IRAN/
PUBLICATION: INDIAN JOURNAL OF MEDICAL RESEARCH SECTION A-INFECTIOUS DISEASES, 1992, V95, MAY (MAY), P115-120
GENUINE ARTICLE#: HX419
LANGUAGE: ENGLISH DOCUMENT TYPE: ARTICLE

ABSTRACT: The occurrence of *colonization"** *factor"** *antigens"** I and II (*CFA"**/I and II) and type 1 somatic pili was investigated in 197 enterotoxigenic Esch, coli (*ETEC"**) isolated from 197 patients of *diarrhoea"** (aged under 3 yr) during February 1985 to March 1986 in Tehran, Iran. Among ETEC strains, 154 strains were heat-stable enterotoxin (ST) producers, 27 strains were *heat"**-*labile"** enterotoxin (*LT"**) producers, and 16 strains produced both toxins. Sixty five (33%) strains showed mannose-resistant haemagglutination (MRHA) of human and/or bovine erythrocytes; of these, 51 (86%) strains were positive for *CFA"**/I and II. Seventy one (36%) strains also exhibited type 1 somatic pili. *CFA"**/I was found in 4 (15%) *LT"** producing, 24 (16%) ST producing, and 2 (13%) *LT"**/ST producing strains. In contrast, *CFA"**/II was only found in ST producing strains (17 strains) and those producing both toxins (4 strains). Patients having *CFAs"**-positive ETEC strains had a significantly

(P<0.001) higher number of stool evacuation per day and a longer duration of diarrhoea than those having *CFAs"**-negative strains. Fifty nine patients had mixed infections of ETEC strains and other enteropathogens. *CFA"**/I or II (*CFAs"**)-positive and *CFAs"**-negative ETEC strains were found in 17 and 42 patients with mixed infections respectively. The mean number of stool evacuations per day was much higher in patients with ETEC and rotavirus than those with only ETEC infection(P<0.001). However, severity of the disease was not affected by the presence or absence of *CFA"**/I or II in ETEC strains found in these patients.

14/3,AB/40 (Item 10 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)

03149610 References: 41
TITLE: EFFICACY OF ENTERIC-COATED PROTEASE IN PREVENTING ATTACHMENT OF *ENTEROTOXIGENIC"** ESCHERICHIA-*COLI"** AND *DIARRHEAL"** DISEASE IN THE RITARD MODEL
AUTHOR(S): MYNOTT TL; CHANDLER DS; LUKE RKJ
CORPORATE SOURCE: LA TROBE UNIV,SCH AGR/BUNDOORA/VIC 3083/AUSTRALIA/ (Reprint); VICTORIAN INST ANIM SCI/ATTWOOD/VIC 3049/AUSTRALIA/
PUBLICATION: INFECTION AND IMMUNITY, 1991, V59, N10 (OCT), P3708-3714
GENUINE ARTICLE#: GH076
LANGUAGE: ENGLISH DOCUMENT TYPE: ARTICLE

ABSTRACT: In this study, we report on a novel approach based on modification of the intestinal surface to prevent *diarrhea"** caused by *enterotoxigenic"** Escherichia *coli"** (*ETEC"**). The removable intestinal tie adult rabbit diarrhea (RITARD) model was used to test the efficacy of an enteric-coated protease preparation (Detach; Enzacor Technology Pty. Ltd.) in the prevention of bacterial attachment and diarrheal disease caused by *colonization"** *factor"** *antigen"** I-positive (*CFA"**/I+) E. coli H10407. Protease was administered orally to rabbits 18 h prior to challenge with 10(11) bacteria. Four groups of rabbits were inoculated with different ETEC strains which produced different combinations of adhesin and enterotoxin or with sterile phosphate-buffered saline. Occurrence of diarrhea during the subsequent 24-h incubation period was recorded. Oral administration of protease was successful in reducing diarrhea and diarrhea-induced death in six of seven (86%) rabbits infected with *CFA"**/I+, heat-stable and *heat"**-*labile"** toxin-positive E. coli (H10407). Seven of eight (87%) rabbits not protected by protease treatment died or developed severe diarrhea. Quantitative analysis of bacterial cultures obtained from the small intestine of rabbits showed a significant (P < 0.001) 2,000-fold reduction in CFU per centimeter of intestine following treatment with protease. The efficacy of protease treatment was 99.5%, with very wide confidence limits (> 0 to 99.9%). The data indicate that the use of protease to prevent *ETEC"** *diarrheal"** disease has considerable potential.

14/3,AB/41 (Item 11 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)

03122461 References: 40
TITLE: *ENTEROTOXIGENIC"** ESCHERICHIA-*COLI"** ASSOCIATED WITH INFANT *DIARRHOEA"** IN GALICIA, NORTH-WESTERN SPAIN

AUTHOR(S): BLANCO J; GONZALEZ EA; BLANCO M; GARABAL JI; ALONSO MP; FERNANDEZ S; VILLANUEVA R; AGUILERA A; GARCIA MA; TORRES J; REY A; JANSEN WH; GUINEE PAM
CORPORATE SOURCE: UNIV SANTIAGO,FAC VET,DEPT MICROBIOL & PARASITOL/LUGO//SPAIN/ (Reprint); RESIDENCIA SANITARIA JUAN CANALEJO,SECC BACTERIOL/LA CORUNA//SPAIN/; HOSPITAL XERAL,UNIDAD MICROBIOL/LUGO//SPAIN/; NATL INST PUBL HLTH & ENVIRONM PROTECT,DEPT BACTERIOL/BILTHOVEN//NETHERLANDS/; HOSP XERAL DE GALICIA,SERV MICROBIOL/SANTIAGO//SPAIN/
PUBLICATION: JOURNAL OF MEDICAL MICROBIOLOGY, 1991, V35, N3 (SEP), P162-167
GENUINE ARTICLE#: GG039
LANGUAGE: ENGLISH DOCUMENT TYPE: ARTICLE

ABSTRACT: To assess the role of *enterotoxigenic"** Escherichia *coli"**(*ETEC"**) in infantile *diarrhoea"**, 482 children with diarrhoea and 103 healthy controls, from three localities of Galicia, northwestern Spain, were investigated between 1985 and 1988. Rotavirus (37.3%) and Salmonella spp. (12.8%) were the most common causal agents, followed by ETEC (3.9%), Campylobacter jejuni (2.3%), Shigella spp. (0.9%) and Yersinia enterocolitica (0.5%). ETEC were significantly more frequently isolated from children with diarrhoea who were under 1 month of age (26.5%) than from older diarrhoeic children (2.2%) ($p < 0.001$) or from healthy children who were under 1 month of age (0%) ($p < 0.05$). Among children who harboured ETEC, five of the nine children under 1 month of age developed diarrhoea in hospital, whereas none of the 10 children over 1 month of age did so. Seventeen ETEC isolates produced heat-stable enterotoxin (STa) only, four produced only *heat"**-*labile"** enterotoxin (*LT"**), and two produced both toxins. *Colonisation"** *factor"** *antigens"** *CFA"**/I and *CFA"**/II were detected in 11 (55.0%) of the 20 ETEC isolates that remained enterotoxigenic after maintenance in the laboratory. Most ETEC isolates belonged to serotypes O153:K - :H45 (nine STa+ *CFA"**/I+ isolates), O27:K - :H7 (three STa+ isolates) or O6:K15:H16 (two *LT"**+ STa+ *CFA"**/II+ isolates). Our results suggest that ETEC constitute an important cause of neonatal diarrhoea in this part of Spain.

14/3,AB/42 (Item 12 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)

03052399 References: 43
TITLE: COLONIZATION FACTORS OF *ENTEROTOXIGENIC"** ESCHERICHIA-*COLI"** ISOLATED FROM CHILDREN WITH *DIARRHEA"** IN ARGENTINA
AUTHOR(S): BINSZTEIN N; JOUVE MJ; VIBOUD GI; MORAL LL; RIVAS M; ORSKOV I; AHREN C; SVENNERHOLM AM
CORPORATE SOURCE: INST NACL MICROBIOL CARLOS G MALBRAN,VELEZ SARSFIELD 563/RA-1281 BUENOS AIRES//ARGENTINA/ (Reprint); STATENS SERUMINST,INT ESCHERICHIA & KLEBSIELLA CTR/DK-2300 COPENHAGEN//DENMARK/; GOTHENBURG UNIV,DEPT MED MICROBIOL & IMMUNOL/S-41346 GOTHENBURG//SWEDEN/
PUBLICATION: JOURNAL OF CLINICAL MICROBIOLOGY, 1991, V29, N9 (SEP), P 1893-1898
GENUINE ARTICLE#: GB716
LANGUAGE: ENGLISH DOCUMENT TYPE: ARTICLE

ABSTRACT: A prospective study was performed to evaluate the presence of *colonization"** *factor"** *antigens"** (*CFAs"**) in enterotoxigenic Escherichia coli (ETEC) strains isolated from 1,211 children with *diarrhea"** in Argentina. One hundred nine *ETEC"** strains that were

isolated from seven different laboratories in various regions of the country were tested for *CFAs"** by using monoclonal antibodies against *CFA"**/I and the E. coli surface antigens CS1, CS2, and CS3 of *CFA"**/II and CS4 and CS5 of *CFA"**/IV; a polyclonal antiserum against CS6 was used. The *CFAs"** searched for were found in 52% of the ETEC strains: 23% of the strains carried *CFA"**/I, 17% carried *CFA"**/IV, and 12% carried *CFA"**/II. All of the *CFA"**/I strains produced heat-stable enterotoxin, and several of them were of the prevalent serotypes O153:H45 and O78:H12. Among the 19 strains expressing *CFA"**/IV, 16 expressed CS5 and CS6 and produced the heat-stable enterotoxin and most were of serotype O128:H21; the remaining 3 strains produced CS6 only. No ETEC strains expressing CS4 were found. Most (11 of 13) of the *CFA"**/II-carrying ETEC strains expressed CS1 and CS3, and 10 of them were of the O6:K15:H16 serotype and produced both *heat"**-*labile"** and heat-stable toxins. As many as 24 of the 109 *CFA"**-negative ETEC strains gave mannose-resistent hemagglutination with erythrocytes from different species; 4 strains had high surface hydrophobicity, suggesting the presence of additional, as yet undefined, colonization factors in up to 25% of the ETEC isolates.

14/3,AB/43 (Item 1 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00614361
USE OF ENZYMES, ESPECIALLY BROMELAIN, IN THE TREATMENT OF NON-INFECTIOUS DIARRHOEA
VERWENDUNG VON ENZYMEN INSBESONDERE BRORELAIN ZUR BEHANDLUNG VON NICHT-INFEKTIOSER DIARRHOE
UTILISATION D'ENZYMES, NOTAMMENT LA BROMELINE, DANS LE TRAITEMENT DE LA DIARRHEE NON-INFECTIEUSE
PATENT ASSIGNEE:
Cortecs (UK) Limited, (930081), Lower Square, Isleworth, Middlesex TW7 6RL, (GB), (Proprietor designated states: all)
INVENTOR:
MYNOTT, Tracey Leahanne, 201 Edgevale Road, Apartment T, Baltimore, MD 21210, (US)
LEGAL REPRESENTATIVE:
Chapman, Paul William et al (73612), Kilburn & Strode, 20 Red Lion Street , London WC1R 4PJ, (GB)
PATENT (CC, No, Kind, Date): EP 671943 A1 950920 (Basic)
EP 671943 B1 990908
WO 9400147 940106
APPLICATION (CC, No, Date): EP 93914851 930630; WO 93GB1374 930630
PRIORITY (CC, No, Date): GB 9213862 920630; GB 9308164 930420; GB 9313189 930625
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FR; GB; GR; IE; IT; LI; LU; MC; NL; PT; SE
INTERNATIONAL PATENT CLASS: A61K-038/45; A61K-038/48
NOTE:
No A-document published by EPO
LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	9936	144
CLAIMS B	(German)	9936	122
CLAIMS B	(French)	9936	154
SPEC B	(English)	9936	5663

Total word count - document A 0
Total word count - document B 6083
Total word count - documents A + B 6083

14/3,AB/44 (Item 2 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00557311
PREPARATION AND USE OF FORMALIN-KILLED *COLONIZATION"**-*FACTOR"**-*ANTIGEN"** (*CFA"**)-EXPRESSING E. COLI ORGANISMS FOR *VACCINATION"** AGAINST ENTERIC INFECTION/DIARRHEA CAUSED
DARSTELLUNG UND VERWENDUNG VON MIT FORMALIN ABGETOTETEN E. COLI BAKTERIEN, DIE DAS KOLONIE-FAKTOR-ANTIGEN (*CFA"**) EXPREMIEREN ZUR IMPFUNG GEGEN DAS DIE DARMINFEKT
PREPARATION ET UTILISATION D'ORGANISMES DE E. COLI TUES DANS LE FORMOL ET EXPRIMANT UN ANTIGENE DE FACTEUR DE COLONISATION (*CFA"**) DANS LE BUT D'UNE *VACCINATION"** C
PATENT ASSIGNEE:
Holmgren, Jan, (1145760), Korvettgatan 1D, S-421 74 Vastra Frolunda, (SE), (applicant designated states:
AT;BE;CH;DE;DK;ES;FR;GB;GR;IT;LI;LU;MC;NL;SE)
SVENNERHOLM, Ann-Mari, (1553120), Korvettgatan 1D, S-421 74 Vastra Frolunda, (SE), (applicant designated states:
AT;BE;CH;DE;DK;ES;FR;GB;GR;IT;LI;LU;MC;NL;SE)
INVENTOR:
Holmgren, Jan, Korvettgatan 1D, S-421 74 Vastra Frolunda, (SE)
SVENNERHOLM, Ann-Mari, Korvettgatan 1D, S-421 74 Vastra Frolunda, (SE)
LEGAL REPRESENTATIVE:
Nilsson, Brita Linnea et al (23742), OSCAR GRAHN PATENTBYRA AB, Box 19540, 104 32 Stockholm, (SE)
PATENT (CC, No, Kind, Date): EP 573527 A1 931215 (Basic)
EP 573527 B1 980909
WO 9214487 920903
APPLICATION (CC, No, Date): EP 92906078 920225; WO 92SE110 920225
PRIORITY (CC, No, Date): SE 91556 910226
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FR; GB; GR; IT; LI; LU; MC; NL; SE
INTERNATIONAL PATENT CLASS: A61K-039/108;
NOTE:
No A-document published by EPO
LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	9837	281
CLAIMS B	(German)	9837	264
CLAIMS B	(French)	9837	321
SPEC B	(English)	9837	5891

Total word count - document A 0
Total word count - document B 6757
Total word count - documents A + B 6757

14/3,AB/45 (Item 3 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00233369
*ORAL"** *VACCINES"**
*ORALE"** IMPFSTOFFE
*VACCINS"** ORAUX
PATENT ASSIGNEE:
BIOTECHNOLOGY AUSTRALIA PTY. LTD., (374170), 28 Barcoo Street, East Roseville, NSW 2069, (AU), (Proprietor designated states: all)
INVENTOR:
RUSSELL-JONES, Gregory, John, 101/2 Artarmon Road, Willoughby, NSW 2068, (AU)
DE AIZPURUA, Henry, James, 9 Douglas Street, Bexley, NSW 2207, (AU)
HOWE, Peter, 6 Mundon Place, West Pennant Hills, NSW 2120, (AU)
RAND, Keith, Norman, 10A Ferncourt Avenue, Chatswood, NSW 2067, (AU)
LEGAL REPRESENTATIVE:
Adkins, Michael et al (42842), Withers & Rogers, Goldings House, 2 Hays Lane, London SE1 2HW, (GB)
PATENT (CC, No, Kind, Date): EP 222835 A1 870527 (Basic)
EP 222835 A1 880323
EP 222835 B1 940928
EP 222835 B2 000419
WO 8606635 861120
APPLICATION (CC, No, Date): EP 86903134 860514; WO 86AU135 860514
PRIORITY (CC, No, Date): AU 85566 850515; AU 853104 851025
DESIGNATED STATES: BE; CH; DE; FR; GB; IT; LI; NL; SE
INTERNATIONAL PATENT CLASS: A61K-039/385; C07K-017/00; C12N-001/20; C12N-015/00
NOTE:
No A-document published by EPO
LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	200016	1870
CLAIMS B	(German)	200016	1774
CLAIMS B	(French)	200016	2210
SPEC B	(English)	200016	8788
Total word count - document A			0
Total word count - document B			14642
Total word count - documents A + B			14642

14/3,AB/46 (Item 1 from file: 357)
DIALOG(R)File 357:Derwent Biotech Res.

0095164 DBA Accession No.: 89-13155
Molecular cloning and characterization of the CS5 and *CFA"** IV fimbrial antigens from enterotoxigenic Escherichia coli (ETEC) - for use in vaccine development (conference abstract)
AUTHOR: Neal B L; Elliot T R; Heuzenroeder M W; Manning P A
CORPORATE SOURCE: Department of Microbiology and Immunology, The University of Adelaide, Adelaide, South Australia, Australia.
JOURNAL: Aust.Microbiol. (9, 2, ASM 13 Meet., 223) 1988
CODEN: 9999Y
LANGUAGE: English
ABSTRACT: Enterotoxigenic Escherichia coli (ETEC) cells have 2 major virulence factors: toxins, which can be either *heat"**-*labile"** (*LT"**) or heat-stable (ST), as well as *colonization"** *factor"** *antigens"** (*CFA"**) also called fimbriae. These factors allow stable

colonization of the gut. The detection of 2 fimbrial types is described: CS5 and *CFA"**/IV. Their molecular cloning, comparative physical properties, NH2-terminal amino acid sequences and genetic organization are also described. The cloning and characterization of these factors may be of use in producing vaccines against *diarrhea"** caused by *ETEC"**. (0 ref)

Set	Items	Description
S15	241	AU=(CARLIN, N? OR CARLIN N?)
S16	39	AU=(ASKELOF, P? OR ASKELOF P?)
S17	22	AU=(BJARE, U? OR BJARE U?)
S18	1	S15 AND S16 AND S17
S19	3	S15 AND (S16 OR S17)
S20	1	S16 AND S17
S21	298	S15 OR S16 OR S17
S22	0	S8 AND S21
S23	3	(S18 OR S19 OR S20) NOT S13
S24	3	RD (unique items)

- Author (s)

>>>No matching display code(s) found in file(s): 65, 113

24/3,AB/1 (Item 1 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS
(c) 2002 European Patent Office. All rts. reserv.

01183250
ORAL VACCINE AGAINST DIARRHEA
ORALER IMPFSTOFF GEGEN DIARRHOE
VACCIN ORAL CONTRE LA DIARRHEE
PATENT ASSIGNEE:
SBL VACCIN AB, (2076680), Lundagatan 2, 105 21 Stockholm, (SE),
(Applicant designated States: all)
INVENTOR:
*CARLIN, Nils"**, Stallknektsgrand 14, S-165 57 Hasselby, (SE)
*ASKELOF, Per"**, Aspvagen 1A, S-191 41 Sollentuna, (SE)
*BJARE, Ulf"**, Noth rsvagen 80, S-757 57 Uppsala, (SE
LEGAL REPRESENTATIVE:
Onn, Thorsten et al (23895), Stockholms Patentbyra Zacco AB P.O. Box 23101, 104 35 Stockholm, (SE)
PATENT (CC, No, Kind, Date): EP 1140159 A1 011010 (Basic)
WO 200037106 000629
APPLICATION (CC, No, Date): EP 99964847 991209; WO 99SE2306 991209
PRIORITY (CC, No, Date): SE 984415 981218
DESIGNATED STATES: AT; BE; CH; CY; DE; DK; ES; FI; FR; GB; GR; IE; IT; LI; LU; MC; NL; PT; SE
EXTENDED DESIGNATED STATES: AL; LT; LV; MK; RO; SI
INTERNATIONAL PATENT CLASS: A61K-039/108
NOTE:
No A-document published by EPO
LANGUAGE (Publication,Procedural,Application): English; English; English

24/3,AB/2 (Item 2 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS
(c) 2002 European Patent Office. All rts. reserv.

00748052
A METHOD OF CULTIVATING BACTERIA PRODUCING PROTEINS THAT ARE EXPRESSED IN A TEMPERATURE REGULATED MANNER

EIN VERFAHREN ZUR KULTIVIERUNG VON BAKTERIEN, DIE PROTEINE HERSTELLEN, DEREN EXPRESSION DURCH TEMPERATUR REGULIERT WIRD
PROCEDE DE CULTURE DE BACTERIES PRODUISANT DES PROTEINES A EXPRESSION REGULEE PAR LA TEMPERATURE
PATENT ASSIGNEE:
SBL VACCIN AB, (2076680), , 105 21 Stockholm, (SE), (applicant designated states: AT;BE;CH;DE;DK;ES;FR;GB;GR;IE;IT;LI;LU;MC;NL;PT;SE)
INVENTOR:
*ASKELOF, Per"**, Aspvagen 1A, 191 41 Sollentuna, (SE)
*CARLIN, Nils"**, Kirunagatan 30, 162 25 Vallingby, (SE)
NILSSON, Bo, Motionsvagen 8, 181 30 Lidingo, (SE)
PAULSSON, Agneta, Lid Lundhagen, 611 91 Nykoping, (SE
LEGAL REPRESENTATIVE:
Nilsson, Brita Linnea et al (23742), OSCAR GRAHN PATENTBYRA AB, Box 19540 , 104 32 Stockholm, (SE)
PATENT (CC, No, Kind, Date): EP 759981 A1 970305 (Basic)
WO 9533825 951214
APPLICATION (CC, No, Date): EP 95921214 950601; WO 95SE628 950601
PRIORITY (CC, No, Date): SE 941921 940603
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FR; GB; GR; IE; IT; LI; LU; MC; NL; PT; SE
INTERNATIONAL PATENT CLASS: C12N-015/00; C12N-001/21; C12N-015/70;
NOTE:
No A-document published by EPO
LANGUAGE (Publication,Procedural,Application): English; English; English

24/3,AB/3 (Item 1 from file: 357)
DIALOG(R)File 357:Derwent Biotech Res.

0192481 DBA Accession No.: 96-02674 PATENT
Temperature regulated cultivation of bacteria expressing surface antigens - temp.-regulated plasmid-mediated Escherichia coli surface antigen expression and fermentation for large-scale recombinant vaccine production
AUTHOR: *Askelof P"**; *Carlin N"**; Nilson B; Paulsson A
CORPORATE SOURCE: Stockholm, Sweden.
PATENT ASSIGNEE: SBL-Vaccin 1995
PATENT NUMBER: WO 9533825 PATENT DATE: 951214 WPI ACCESSION NO.: 96-058138 (9606)
PRIORITY APPLIC. NO.: SE 941921 APPLIC. DATE: 940603
NATIONAL APPLIC. NO.: WO 95SE628 APPLIC. DATE: 950601
LANGUAGE: English
ABSTRACT: A method is claimed for the cultivation of bacteria containing plasmids consisting of genes encoding surface or membrane-bound antigens or other proteins which are expressed in a temp.-regulated manner for the production of desired bacterial products, involving: (a) culture of the bacteria in a medium at a temp. such that the bacteria retain their plasmids, but no expression occurs (preferably at room temp., specifically at approximately 20 deg); (b) further culture of the inoculum in a medium at a temp. at which expression occurs (preferably at the body temp. of a mammal, specifically at 34-39 deg); (c) harvesting of the bacteria prior to them losing the plasmids; and (d) isolation of the desired product. Preferably the bacterium is Escherichia coli expressing at least one type of colonization factor antigen selected from CFA/I, CS1, CS2, CS3, CS4, CS5 and CS6. This method is used to produce commercial quantities of E. coli with intact

colonization factor antigens and sub-components in large-scale industrial fermentors. The bacteria can be inactivated and used to prepare recombinant vaccines against E. coli. (10pp)

? log y

Devi, S.
09/868243

(FILE 'CAPLUS' ENTERED AT 10:51:23 ON 31 MAY 2002)

L5 281 SEA FILE=CAPLUS ABB=ON PLU=ON (ETEC OR (ENTEROTOX? OR ENTERO TOX?)(5A)COLI)(5A)DIARRH?

L6 40 SEA FILE=CAPLUS ABB=ON PLU=ON L5 AND (CFA## OR COLON? FACTOR ANTIGEN)

L7 23 SEA FILE=CAPLUS ABB=ON PLU=ON L6 AND (VACCIN? OR IMMUNIS? OR IMMUNIZ?)

L11 4 SEA FILE=CAPLUS ABB=ON PLU=ON L7 AND (LT OR HEAT LABILE)

L5 281 SEA FILE=CAPLUS ABB=ON PLU=ON (ETEC OR (ENTEROTOX? OR ENTERO TOX?)(5A)COLI)(5A)DIARRH?

L6 40 SEA FILE=CAPLUS ABB=ON PLU=ON L5 AND (CFA## OR COLON? FACTOR ANTIGEN)

L7 23 SEA FILE=CAPLUS ABB=ON PLU=ON L6 AND (VACCIN? OR IMMUNIS? OR IMMUNIZ?)

L12 14 SEA FILE=CAPLUS ABB=ON PLU=ON L7 AND (ORAL? OR MOUTH OR PER OS)

L13 15 L11 OR L12

L13 ANSWER 1 OF 15 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2002:150589 CAPLUS

DOCUMENT NUMBER: 136:293151

TITLE: Transcutaneous **immunization** using colonization factor and **heat-labile** enterotoxin induces correlates of protective immunity for enterotoxigenic Escherichia coli

AUTHOR(S): Yu, Jianmei; Cassels, Frederick; Scharton-Kerstein, Tanya; Hammond, Scott A.; Hartman, Antoinette; Angov, Evelina; Corthesy, Blaise; Alving, Carl; Glenn, Gregory

CORPORATE SOURCE: Department of Membrane Biochemistry, Walter Reed Army Institute of Research, Silver Spring, MD, USA

SOURCE: Infection and Immunity (2002), 70(3), 1056-1068
CODEN: INFIBR; ISSN: 0019-9567

PUBLISHER: American Society for Microbiology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB **Enterotoxigenic** Escherichia **coli** (**ETEC**) **diarrheal** disease is a worldwide problem that may be addressed by transcutaneous delivery of a **vaccine**. In several human settings, protective immunity has been assocd. with immune responses to E. coli colonization factors and to the **heat-labile** toxin that induces the diarrhea. In this set of animal studies, transcutaneous **immunization** (TCI) using recombinant colonization factor CS6 and cholera toxin (CT) or **heat-labile** enterotoxin (**LT**) as the adjuvant induced IgG and IgA anti-CS6 responses in sera and stools and antibody responses that recognized CS6 antigen in its native configuration. The antitoxin immunity induced by TCI was also shown to protect against enteric toxin challenge. Although **immunization** with **LT** via the skin induced mucosal

secretory IgA responses to **LT**, protection could also be achieved by i.v. injection of the immune sera. Finally, a malaria **vaccine** antigen, merozoite surface protein 142 administered with CT as the adjuvant, induced both merzoite surface protein antibodies and T-cell responses while conferring protective antitoxin immunity, suggesting that both antiparasitic activity and antidiarrheal activity can be obtained with a single **vaccine** formulation. Overall, the results demonstrate that relevant colonization factor and antitoxin immunity can be induced by TCI and suggest that an **ETEC** traveler's **diarrhea** **vaccine** could be delivered by using a patch.

REFERENCE COUNT: 51 THERE ARE 51 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 2 OF 15 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:549212 CAPLUS
DOCUMENT NUMBER: 136:198489
TITLE: Construction and characterization of genetically defined aro omp mutants of enterotoxigenic Escherichia coli and preliminary studies of safety and immunogenicity in humans
AUTHOR(S): Turner, Arthur K.; Terry, Tamsin D.; Sack, David A.; Londono-Arcila, Patricia; Darsley, Michael J.
CORPORATE SOURCE: Acambis Ltd., Cambridge, CB1 9PT, UK
SOURCE: Infection and Immunity (2001), 69(8), 4969-4979
CODEN: INFIBR; ISSN: 0019-9567
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Enterotoxigenic Escherichia coli (**ETEC**) is a leading cause of **diarrhea** in travelers to countries where the disease is endemic and causes a major disease burden in the indigenous population, particularly children. The authors describe here the generation and preclin. characterization of candidate strains of ETEC which are intended to provide the basis of a live attenuated **oral vaccine** to prevent this disease. It has been shown previously that a spontaneously arising toxin-neg. variant ETEC strain, E1392/75-2A, could confer 75% protection against challenge when administered to volunteers. Unfortunately this strain induced mild diarrhea in 15% of recipients. To eliminate the unacceptable reactogenicity of strain E1392/75-2A, it was further attenuated by introducing three different combinations of defined deletion mutations into the chromosome. A mouse intranasal model of **immunization** was developed and used to show that all of the strains were immunogenic. Immune responses against **colonization factor antigens** (**CFAs**) were particularly strong when the bacterial inocula were grown on "**CFA** agar," which induces strong expression of these antigens. Two of the strains were selected for a phase I dose escalation safety study with healthy adult volunteers. Freshly grown organisms were harvested from **CFA** agar plates and administered to volunteers as a suspension contg. from 5 .times. 107 to 5 .times. 109 CFU. The **vaccine** was well tolerated at all doses and induced significant immune responses in all recipients at the highest dose of either strain. The results provide the basis for further clin. evaluation of these **vaccine** candidates.

REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 3 OF 15 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:519976 CAPLUS
DOCUMENT NUMBER: 133:227633
TITLE: Safety and immunogenicity of two different lots of the **oral**, killed enterotoxigenic Escherichia coli-cholera toxin B subunit **vaccine** in Israeli young adults
AUTHOR(S): Cohen, Dani; Orr, Nadav; Haim, Moti; Ashkenazi, Shai; Robin, Guy; Green, Manfred S.; Ephros, Moshe; Sela, Tamar; Slepon, Raphael; Ashkenazi, Isaac; Taylor, David N.; Svennerholm, Ann-Mari; Eldad, Arieh; Shemer, Joshua
CORPORATE SOURCE: Army Health Branch Research Unit, Medical Corps, Israel Defence Force, Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv-Jaffa, Israel
SOURCE: Infection and Immunity (2000), 68(8), 4492-4497
CODEN: INFIBR; ISSN: 0019-9567
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Enterotoxigenic Escherichia coli (ETEC) is one of the leading causes of diarrhea among Israeli soldiers serving in field units. Two double-blind placebo-controlled, randomized trials were performed among 155 healthy volunteers to evaluate the safety and immunogenicity of different lots of the **oral**, killed ETEC **vaccine** consisting of two doses of whole cells plus recombinantly produced cholera toxin B subunit (rCTB). The two doses of **vaccine** lot E005 and the first dose of **vaccine** lot E003 were well tolerated by the volunteers. However, 5 (17%) **vaccinees** reported an episode of vomiting a few hours after the second dose of lot E003; none of the placebo recipients reported similar symptoms. Both lots of **vaccine** stimulated a rate of significant antibody-secreting cell (ASC) response to CTB and to **colonization factor antigen** I (**CFA**/I) after one or two doses, ranging from 85 to 100% and from 81 to 100%, resp. The rate of ASC response to CS2, CS4, and CS5 was slightly lower than the rate of ASC response induced to CTB, **CFA**/I, and CS1. The second **vaccine** dose enhanced the response to CTB but did not increase the frequencies or magnitude of ASC responses to the other antigens. The two lots of the ETEC **vaccine** induced similar rates of serum antibody responses to CTB and **CFA**/I which were less frequent than the ASC responses to the same antigens. Based on these safety and immunogenicity data, an efficacy study of the ETEC **vaccine** is under way in the Israel Defense Force.
REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 4 OF 15 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:441654 CAPLUS
DOCUMENT NUMBER: 133:64009

TITLE: **Oral vaccine** against diarrhea
INVENTOR(S): Carlin, Nils; Askelof, Per; Bjare, Ulf
PATENT ASSIGNEE(S): SBL Vaccin AB, Swed.
SOURCE: PCT Int. Appl., 11 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000037106	A1	20000629	WO 1999-SE2306	19991209
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
SE 9804415	A	20000619	SE 1998-4415	19981218
SE 515285	C2	20010709		
BR 9916278	A	20010904	BR 1999-16278	19991209
EP 1140159	A1	20011010	EP 1999-964847	19991209
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
NO 2001002889	A	20010612	NO 2001-2889	20010612

PRIORITY APPLN. INFO.: SE 1998-4415 A 19981218
WO 1999-SE2306 W 19991209

AB An **oral vaccine** compn. against **enterotoxigenic** E. **coli** caused **diarrhea** in humans is disclosed. It comprises a defined amt. of at least three different types of **colonization factor antigens** (**CFAs**), e.g. 100 to 300 .mu.g of each type, selected from the group consisting of **CFA** I, **CFA** II (CS1, CS2 and CS3) and **CFA** IV (CS4, CS5 and CS6), on killed E. coli bacteria lacking the gene encoding the **heat labile** enterotoxin (**LT**-), together with a defined amt. of the B-subunit of cholera toxin (CTB), e.g. 0.5-2.0 mg, and a vehicle, such as PBS, which **vaccine** compn. is purified from possible heat stable enterotoxin (ST).

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 5 OF 15 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:768665 CAPLUS
DOCUMENT NUMBER: 132:62841
TITLE: Intestinal immune responses in patients infected with enterotoxigenic Escherichia coli and in **vaccinees**
AUTHOR(S): Wenneras, Christine; Qadri, Firdausi; Bardhan, Prodeep K.; Sack, R. Bradley; Svennerholm, Ann-Mari
CORPORATE SOURCE: Department of Medical Microbiology and

Immunology, Goteborg University, Goteborg, 413 46, Swed.
SOURCE: Infection and Immunity (1999), 67(12), 6234-6241
CODEN: INFIBR; ISSN: 0019-9567
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Immune responses against enterotoxigenic Escherichia coli (ETEC) were examd. in Bangladeshi adults with naturally acquired disease and compared to responses in age-matched Bangladeshi volunteers who had been **orally immunized** with a **vaccine** consisting of inactivated ETEC bacteria expressing different **colonization factor antigens** (CFs) and the B subunit of cholera toxin. B-cell responses in duodenal biopsy samples, feces, intestinal washings, and blood were detd. Because most of the patients included in the study were infected with ETEC expressing CS5, immune responses to this CF were studied most extensively. **Vaccinees** and patients had comparable B-cell responses against this antigen in the duodenum: the median nos. of antibody-secreting cells (ASC) were 3300 IgA ASC/107 mononuclear cells (MNC) in the patient group and 1200 IgA ASC/107 MNC in the **vaccinees** (not a significant difference). Similarly, no statistically significant differences were seen in the levels of duodenal B cells directed against enterotoxin among **vaccines** and patients. A comparison of the capacities of the various methods used to assess mucosal immune responses revealed a correlation between nos. of circulating B cells and antibody levels in saponin exts. of duodenal biopsy samples (r = 0.58) after **vaccination**. However, no correlation was seen between blood IgA ASC and duodenal IgA ASC after two doses of **vaccine**. Still, a correlation between nos. of CF-specific B cells in blood sampled from patients early during infection and nos. of duodenal B cells collected 1 wk later was apparent (r = 0.70).

REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 6 OF 15 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1999:761959 CAPLUS
DOCUMENT NUMBER: 132:45567

TITLE: Expression of CS3 from enterotoxigenic Escherichia coli in Shigella flexneri 2a and immunogenicity of the recombinant strain

AUTHOR(S): Han, Zhaozhong; Ying, Tianyi; Cao, Yong; Rui, Xianliang; Zhang, Zhaoshan; Su, Guofu; Huang, Cuifen
CORPORATE SOURCE: Beijing Institute of Biotechnology, Beijing, 100071, Peop. Rep. China

SOURCE: Zhongguo Shengwu Huaxue Yu Fenzi Shengwu Xuebao (1999), 15(5), 719-723
CODEN: ZSHXF2; ISSN: 1007-7626
PUBLISHER: Zhongguo Shengwu Huaxue Yu Fenzi Shengwu Xuebao Bianweihui
DOCUMENT TYPE: Journal
LANGUAGE: Chinese

AB A host-plasmid balancing system was established based on asd gene in a candidate **vaccine** strain(T32) of Shigella flexneri 2a. Asd gene of T32 was amplified by polymerase chain reaction(PCR), and

its structural gene fragment was replaced by human interleukin 2 gene. The mutated asd gene was introduced to T32 genome by homol. recombination. The resulted bacteria strain (FaD) was used as antigen carrier to express E. coli surface antigen CS3 of enterotoxigenic E. coli, which was expressed on a complementory plasmid carrying asd gene from Streptococcus mutans. The plasmid could stably be maintained and expressed CS3 in the host cell without any antibiotic selection. Antibodies against CS3 could be detected in sera of mice **immunized** with recombinant bacteria either **orally** or s.c., and mice **immunized** by either route could be protected from challenging with virulent strain of the same serotype. All results indicate that the recombinant constructed can be used as bi-valent **vaccine** candidate for prevention of bacterial diarrhea.

L13 ANSWER 7 OF 15 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:414008 CAPLUS
DOCUMENT NUMBER: 129:147825
TITLE: Intestinal immune responses to an inactivated **oral** enterotoxigenic Escherichia coli **vaccine** and associated immunoglobulin A responses in blood
AUTHOR(S): Ahren, Christina; Jertborn, Marianne; Svennerholm, Ann-Mari
CORPORATE SOURCE: Departments of Medical Microbiology and Immunology, Goteborg University, Goteborg, S-413 46, Swed.
SOURCE: Infection and Immunity (1998), 66(7), 3311-3316 CODEN: INFIBR; ISSN: 0019-9567
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB An inactivated **oral enterotoxigenic** E. **coli (ETEC) vaccine** against **ETEC diarrhea** was given to 25 adult Swedish volunteers. The **vaccine** consisted of formalin-killed E. coli bacteria expressing the most common **colonization factor antigens (CFAs)**, i.e., **CFA**/I, -II, and -IV, and recombinantly produced cholera B subunit (CTB). IgA antibody responses in intestinal lavage fluid to CTB and **CFAs** were detd. and compared with corresponding responses in stool exts. and serum as well as with IgA antibody-secreting cell (ASC) responses in peripheral blood. Two doses of **vaccine** induced IgA responses to the different **CFAs** in lavage fluid in 61-87% of the **vaccinees** and in stool in 38-81% of them. The most frequent responses were seen against **CFA**/I. The magnitudes of the antibody responses against CTB and **CFA**/I in stool correlated with those in intestinal lavage. Intestinal lavage responses against **CFAs** were best reflected by the ASC responses, with the sensitivity of the ASC assay being 80-85%, followed by stool (sensitivity of 50-88%) and serum antibody (sensitivity of 7-65%) analyses. CTB-specific immune responses were seen in >90% of the **vaccinees** in all assays.

L13 ANSWER 8 OF 15 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1996:91410 CAPLUS
DOCUMENT NUMBER: 124:172822

TITLE: Optimization of the intestinal lavage procedure for determination of intestinal immune responses
AUTHOR(S): Aahren, Christina; Andersson, Kerstin; Wiklund, Gudrun; Wenneraas, Christine; Svennerholm, Ann-Mari
CORPORATE SOURCE: Dep. Medical Microbiology Immunology, Goeteborg Univ., Goeteborg, Swed.
SOURCE: Vaccine (1995), 13(18), 1754-8
CODEN: VACCDE; ISSN: 0264-410X
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Optimal conditions to process, conc. and store intestinal lavage fluid were studied in samples collected from volunteers before and after **oral immunization** with a prototype **vaccine** against **enterotoxigenic** Escherichia **coli** (**ETEC**) **diarrhea**. Total IgA and specific IgA antibody titers against enterotoxin and **colonization factor antigen** were detd. in 22 lavage samples which were either enzyme-inhibited or heat-inactivated and then subjected to different long-term storage conditions. Samples were analyzed within 1 mo of collection and also after 3, 6, and 24 mo of storage. Total IgA concns. and specific IgA antibody levels were higher in lavage samples treated with enzyme inhibitors (soybean trypsin inhibitor and phenylmethylsulfonyl fluoride) than in those heat-inactivated. Similarly, concn. of the lavage fluid by freeze-drying was superior to concn. against polyethylene glycol. Specific antibody titers remained elevated after storage for at least 6 mo but declined after 2 yr in frozen compared with freeze-dried samples.

L13 ANSWER 9 OF 15 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1995:840282 CAPLUS
DOCUMENT NUMBER: 123:283084
TITLE: Simultaneous expression of **CFA**/I and CS3 **colonization factor antigens** of enterotoxigenic Escherichia coli by .DELTA.aroC, .DELTA.aroD Salmonella typhi **vaccine** strain CVD 908
AUTHOR(S): Giron, Jorge A.; Xu, Jian-Guo; Gonzalez, Cesar R.; Hone, David; Kaper, James B.; Levine, Myron M.
CORPORATE SOURCE: School Medicine, University Maryland, Baltimore, MD, 21201, USA
SOURCE: Vaccine (1995), 13(10), 939-46
CODEN: VACCDE; ISSN: 0264-410X
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Among the known colonization factors of enterotoxigenic Escherichia coli (ETEC), **CFA**/I and CS3 (the common antigen in the **CFA**/II family of fimbrial antigens) are two of the most prevalent fimbrial antigens found in clin. isolates but are never expressed by the same wild-type strain. We manipulated the genetic determinants encoding CS3 and **CFA**/I fimbriae so that these two important colonization factors are expressed simultaneously in attenuated Salmonella typhi live **oral vaccine** strain CVD 908, including after growth in liq. medium (**CFA**/I is poorly expressed by wild-type ETEC in broth culture). The recombinant fimbrial structures produced by CVD 908 are morphol.

indistinguishable from the CS3 fibrillae and **CFA**/I rod-like fimbriae produced by ETEC, and are recognized by monospecific CS3 and **CFA**/I antibodies. This prototype construct may prove useful in investigating the live vector approach to immunoprophylaxis of **ETEC diarrheal** disease.

L13 ANSWER 10 OF 15 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1994:503944 CAPLUS
DOCUMENT NUMBER: 121:103944
TITLE: Molecular characterization of enterotoxigenic Escherichia coli (ETEC) isolated in New Caledonia (value of potential protective antigens in **oral vaccine** candidates)
AUTHOR(S): Begaud, E.; Mondet, D.; Germani, Y.
CORPORATE SOURCE: Enteric Pathog. Lab., Inst. Pasteur Nouvelle-Caledonie, Noumea, New Caledonia
SOURCE: Res. Microbiol. (1993), 144(9), 721-8
CODEN: RMCREW; ISSN: 0923-2508
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The role of **enterotoxigenic** Escherichia **coli** (**ETEC**) in childhood **diarrhea** in New Caledonia has been demonstrated in previous epidemiol. works. This study was undertaken in order to characterize these strains and to det. whether bacterial components of current **vaccine** candidates (toxin, **colonization factor antigens**, O:H antigens) would be useful in the authors' region. Some 24 ETEC strains were studied; 5 strains produced **heat-labile** enterotoxin, 17 strains produced heat-stable enterotoxin (9 STp and 8 STh), and 2 strains produced both toxins (1 **LT**/STp/STh and 1 **LT**/STh). E. coli strains were screened for the presence of genes encoding for enterotoxins (DNA dot blot and Southern hybridization assays); the results obtained with probes were closely correlated and were in agreement with biol. assays. No two ETEC strains possessed similar plasmid profiles, and DNA sequences encoding for enterotoxins were located on plasmids ranging from 58 to 75 MDa. The O:H (O1:H-,O2:H7, O6:H16, O25:H-, O27:H7, O28ab:H9, O52:H10, O64:H5, O70:H-, O78:H12, O88:H25, O99:H6, O101:H-, O126:H12, O166:H30) serotypes are presented (all the strains were typable, but some ETEC serotypes were unusual). By using antisera against **colonization factor antigens** (**CFA**) I and II, results showed that 9 of the 24 ETEC strains expressed **CFA** (2 **CFA**/II and 7 **CFA**/I). These strains possessed high bacterial surface hydrophobicity. Fifteen ETEC did not possess **CFA**; among these, 11 did not exhibit high hydrophobicity or show hemagglutination activity. Four of the 15 **CFA**-neg. strains exhibited high hydrophobicity (two O64:H45, one O70:H- and one O88:H25) but no hemagglutination in the presence or absence of mannose. Only 7 of 24 ETEC expressed resistance to ampicillin, trimethoprim-sulfamethoxazole or tetracycline. The data indicate that several ETEC isolates would be refractory to current **vaccine** candidates, and that for **vaccines** to be effective in the authors' region, other antigens must be included.

L13 ANSWER 11 OF 15 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1993:601340 CAPLUS

DOCUMENT NUMBER: 119:201340
TITLE: Intestinal antibody response after **oral immunization** with a prototype cholera B subunit-**colonization factor antigen** enterotoxigenic Escherichia coli **vaccine**
AUTHOR(S): Aahren, Christina; Wenneraas, Christine; Holmgren, Jan; Svennerholm, Ann Mari
CORPORATE SOURCE: Dep. Med. Microbiol. Immunol., Univ. Goeteborg, Goeteborg, S-413 46, Swed.
SOURCE: Vaccine (1993), 11(9), 929-34
CODEN: VACCDE; ISSN: 0264-410X
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A prototype **oral** enterotoxigenic Escherichia coli (ETEC) **vaccine** contg. formalin-inactivated whole bacteria expressing **colonization factor antigens** **CFA**/I and **CFA**/II and cholera B subunit (CTB) was tested for safety and immunogenicity in 20 adult Swedish volunteers. When given in three doses with 2-wk intervals the **vaccine** was found to be safe and to give rise to specific IgA antibody responses in intestinal lavage fluid in most of the volunteers (**CFA**/I 82%, **CFA**/II 82% and CTB 91%). The frequencies and magnitudes of these responses, which were already maximal after two doses, were comparable with thoses previously found in patients convalescing from severe **ETEC** **diarrhea**. All the **vaccinated** volunteers also responded with antitoxin IgA as well as IgG antibodies in serum, whereas the serum antibody responses against the **CFAs** were weaker and mainly of the IgA isotype.

L13 ANSWER 12 OF 15 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1992:639820 CAPLUS
DOCUMENT NUMBER: 117:239820
TITLE: Preparation and use of formalin-killed **colonization-factor-antigen** (**CFA**)-expressing Escherichia coli for **vaccination** against enteric infection/**diarrhea** caused by **enterotoxigenic** E. **coli** in humans
INVENTOR(S): Holmgren, Jan; Svennerholm, Ann Mari
PATENT ASSIGNEE(S): Swed.
SOURCE: PCT Int. Appl., 44 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9214487	A1	19920903	WO 1992-SE110	19920225
W: AU, BB, BG, BR, CA, CS, FI, HU, JP, KP, KR, LK, MG, MN, MW, NO, PL, RO, RU, SD, US				
RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GN, GR, IT, LU, MC, ML, MR, NL, SE, SN, TD, TG				
CA 2014877	AA	19920827	CA 1992-2104877	19920225

AU 9213308	A1	19920915	AU 1992-13308	19920225
AU 663864	B2	19951026		
EP 573527	A1	19931215	EP 1992-906078	19920225
EP 573527	B1	19980909		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, MC, NL, SE				
BR 9205677	A	19940517	BR 1992-5677	19920225
JP 06505730	T2	19940630	JP 1992-506105	19920225
JP 3169608	B2	20010528		
HU 67198	A2	19950228	HU 1993-2410	19920225
HU 213924	B	19971128		
RO 109819	B1	19950630	RO 1993-1142	19920225
CZ 281556	B6	19961113	CZ 1993-1742	19920225
AT 170755	E	19980915	AT 1992-906078	19920225
ES 2123550	T3	19990116	ES 1992-906078	19920225
RU 2127121	C1	19990310	RU 1993-53899	19920225
SK 280919	B6	20000912	SK 1993-910	19920225
NO 9303037	A	19930825	NO 1993-3037	19930825
PRIORITY APPLN. INFO.:			SE 1991-556 A	19910226
			WO 1992-SE110 A	19920225

AB E. coli strain selected from different known strains each having the ability of expressing a certain type of **CFA** antigens, is grown in a liq. culture allowing high-level expression of the certain type of **CFA** on the surface of the E. coli to a predetd. d., followed by harvesting and resuspension of the bacterial culture in saline, whereupon formalin is added to the suspension to a final concn. of 0.2 M, followed by incubation at 37.degree. for 2 hs and at 4.degree. for 24-48 hs, resulting in a formalin-killed E. coli. Procedures are detailed for achieving high level expression of **CFAs** on E. coli grown in a liq. medium. The liq.-grown formalin-inactivated **CFAs** on E. coli were **orally** administered to human volunteers and stimulation of IgA antibody formation in intestinal lavage fluid was obsd.

L13 ANSWER 13 OF 15 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER:	1985:576728 CAPLUS
DOCUMENT NUMBER:	103:176728
TITLE:	Experimental **enterotoxin**-induced Escherichia **coli diarrhea** and protection induced by previous infection with bacteria of the same adhesin or enterotoxin type
AUTHOR(S):	Aahren, Christina M.; Svennerholm, Ann Mari
CORPORATE SOURCE:	Dep. Med. Microbiol., Univ. Goeteborg, Goeteborg, S-413 46, Swed.
SOURCE:	Infect. Immun. (1985), 50(1), 255-61 CODEN: INFIBR; ISSN: 0019-9567
DOCUMENT TYPE:	Journal
LANGUAGE:	English

AB The diarrheal response to an initial and a second infection with E. coli expressing various enterotoxins (the heat-stable toxin [ST] alone or in combination with the **heat-labile** toxin [**LT**]) and **colonization factor antigens** (**CFA**/I, **CFA**/II, or E87725-type) was studied in the reversible tie adult rabbit diarrhea model. An initial infection with high doses (1 .times. 1010 to 5 .times. 1011 bacteria) of the various strains regularly induced diarrhea which was usually self-limiting. The diarrheal response to equally EDs of

different strains producing both ST and **LT** (ST/**LT**) did not differ significantly with serotype or **colonization factor antigen**. ST/**LT**-producing strains appeared to induce severe disease more regularly than ST-producing strains carrying the same adhesin. Previous infection with **CFA**/I-carrying, ST/**LT**-producing E. coli protected all animals reinfected with an otherwise highly diarrheogenic dose of the same strain as well as against challenge with a **CFA**/I-carrying, ST/**LT**-producing strain with different O-, K-, and H-antigens. Fecal excretion of bacteria was also decreased in the protected animals, although not completely eliminated. When only 1 of the 2 antigens, **CFA**/I and **LT**, was shared by the **immunizing** and rechallenge strains, partial protection was evident consistent with independent antibacterial (anti-**CFA**) and antitoxic (anti-**LT**) immune mechanisms. **Oral immunization** with purified **CFA**/I decreased fluid secretion in intestinal loops infected with **CFA**/I-carrying enterotoxigenic bacteria.

L13 ANSWER 14 OF 15 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1985:4249 CAPLUS
DOCUMENT NUMBER: 102:4249
TITLE: Enterotoxigenic Escherichia coli pathogenic for man: biological and immunological aspects of fimbrial **colonization factor antigens**
AUTHOR(S): Evans, Dolores G.; Evans, Doyle J., Jr.; Sack, David A.; Clegg, Steven
CORPORATE SOURCE: Med. Sch., Univ. Texas, Houston, TX, USA
SOURCE: Attachment Org. Gut Mucosa, [Pap. Res. Workshop] (1984), Meeting Date 1981, Volume 1, 63-78. Editor(s): Boedeker, Edgar C. CRC: Boca Raton, Fla.
CODEN: 52SOA7
DOCUMENT TYPE: Conference
LANGUAGE: English
AB The role of **colonization factor antigens** (**CFA**) in the immune response in man which protects against infections with enterotoxigenic E. coli (ETEC) was studied. Parenterally administered **CFA**/I induced specific IgG responses to differing degrees in 5 volunteers. **Oral** re-exposure to **CFA**/I-pos. ETEC did not result in illness or seroconversion 1 yr after initial exposure. Anti-**CFA** secretory IgA in human milk as a result of exposure to ETEC was found in 74% of the samples from Dacca, Bangladesh and in 20% of those from Houston, Texas. The latter figure indicates that **ETEC diarrhea** might be more common than is indicated by sampling infants for diarrhea.

L13 ANSWER 15 OF 15 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1979:538707 CAPLUS
DOCUMENT NUMBER: 91:138707
TITLE: Purification and characterization of the **CFA**/I antigen of enterotoxigenic Escherichia coli
AUTHOR(S): Evans, Dolores G.; Evans, Doyle J., Jr.; Clegg, Steven; Pauley, Judith A.
CORPORATE SOURCE: Med. Sch., Univ. Texas, Houston, TX, 77030, USA

SOURCE: Infect. Immun. (1979), 25(2), 738-48
CODEN: INFIBR; ISSN: 0019-9567
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The fimbrial **colonization factor antigen** I (**CFA**/I) of enterotoxigenic Escherichia coli was purified and characterized. The initial purifn. step was release of these fimbriae from the bacterial cells by homogenization with a Waring blender. Common fimbriae and flagellar antigen were avoided by careful control of growth conditions and the use of a nonmotile (H-) mutant of the prototype strain H-10407 (078:H11). The essential purifn. steps were membrane filtration, ammonium sulfate fraction, and neg. dimethylaminoethyl-Sephadex column chromatog. Yields were .apprx.4.0 mg of **CFA**/I protein/g bacteria. Purified **CFA**/I was a fimbrial mol. 7.0 nm in diam. and had an av. mol. wt. of 1.6 .times. 106, as detd. by sedimentation equil. **CFA**/I was a polymer of identical subunits of mol. wt. 23,800 with an N-terminal valine, 37% hydrophobic amino acid residues, and 11 residues of proline/mol. The purified antigen retained its morphol., antigenicity, and biol. activity. Purified **CFA**/I exhibited mannose-resistant hemagglutination of human group A, bovine, and chicken erythrocytes, as do **CFA**/I-pos. bacteria. **CFA**/I detached from the bacteria was monovalent; however, purified **CFA**/I antigen retained an affinity for the epithelial cells of rabbit small intestine and blocked adhesion of **CFA**/I-pos. bacteria. Thus, purified **CFA**/I is a good candidate for use in an **oral vaccine** for immunoprotection against **diarrhea** caused by **CFA**/I-pos. **enterotoxigenic** E. **coli**.

[redacted], BIOSIS, EMBASE, WPIDS, JICST-EPLUS, JAPIO, PHIC, PHIN, TOXCENTER' ENTERED AT 10:53:57 ON 31 MAY 2002)

L5 281 SEA FILE=CAPLUS ABB=ON PLU=ON (ETEC OR (ENTEROTOX? OR ENTERO TOX?)(5A)COLI)(5A)DIARRH?
L6 40 SEA FILE=CAPLUS ABB=ON PLU=ON L5 AND (CFA## OR COLON? FACTOR ANTIGEN)
L7 23 SEA FILE=CAPLUS ABB=ON PLU=ON L6 AND (VACCIN? OR IMMUNIS? OR IMMUNIZ?)
L8 118 SEA L7
L9 59 SEA L8 AND (LT OR HEAT LABILE)

L5 281 SEA FILE=CAPLUS ABB=ON PLU=ON (ETEC OR (ENTEROTOX? OR ENTERO TOX?)(5A)COLI)(5A)DIARRH?
L6 40 SEA FILE=CAPLUS ABB=ON PLU=ON L5 AND (CFA## OR COLON? FACTOR ANTIGEN)
L7 23 SEA FILE=CAPLUS ABB=ON PLU=ON L6 AND (VACCIN? OR IMMUNIS? OR IMMUNIZ?)
L8 118 SEA L7
L14 69 SEA L8 AND (ORAL? OR MOUTH OR PER OS)

L15 94 L9 OR L14

PROCESSING COMPLETED FOR L15

Searcher : Shears 308-4994

L16 35 DUP REM L15 (59 DUPLICATES REMOVED)

L16 ANSWER 1 OF 35 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 2002246664 MEDLINE
DOCUMENT NUMBER: 21981403 PubMed ID: 11985274
TITLE: Simultaneous expression of CS3 **colonization factor antigen** and **LT** -B/ST fusion enterotoxin antigen of enterotoxigenic Escherichia coli by attenuated Salmonella typhimurium.
AUTHOR: Xu Bing; Zhang Zhao-Shan; Li Shu-Qin; Shu Dong; Huang Cui-Fen
CORPORATE SOURCE: Beijing Institute of Biotechnology, 20 Dong Dajie Street, Fengtai District, Beijing 100071, China.. bingxx@hotmail.com
SOURCE: I CHUAN HSUEH PAO. ACTA GENETICA SINICA, (2002 Apr) 29 (4) 370-6.
Journal code: 7900784. ISSN: 0379-4172.
PUB. COUNTRY: China
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200205
ENTRY DATE: Entered STN: 20020503
Last Updated on STN: 20020517
Entered Medline: 20020516

AB **LT** and ST are the main enterotoxins of enterotoxigenic Escherichia coli (ETEC) found in clinical isolates, and CS3 (the common antigen in the **CFA**/II family of fimbrial antigens) is one of the most prevalent antigens of colonization factors. The genetic determinants encoding CS3 and **LT**-B/ST fusion toxin were manipulated so that these important antigens are expressed simultaneously in attenuated Salmonella typhimurium **oral vaccine** strain X4072. These antigens produced by X4072 (pXZL88) could be recognized with monospecific CS3, **LT** or ST antibodies respectively. The specific antibodies against CS3, **LT** and ST could be detected. In the sera of **immunized** mice via **oral** route with the live bacteria. Significantly, the antibody to ST was able to neutralize the biological activity of native ST. This prototype construct may be proved to be useful in investigating the live vector approach to immunoprophylaxis of **ETEC diarrhea** disease.

L16 ANSWER 2 OF 35 MEDLINE DUPLICATE 2
ACCESSION NUMBER: 2001392806 MEDLINE
DOCUMENT NUMBER: 21340384 PubMed ID: 11447175
TITLE: Construction and characterization of genetically defined aro omp mutants of enterotoxigenic Escherichia coli and preliminary studies of safety and immunogenicity in humans.
COMMENT: Erratum in: Infect Immun 2001 Oct;69(10):6564
AUTHOR: Turner A K; Terry T D; Sack D A; Londono-Arcila P; Darsley M J
CORPORATE SOURCE: Acambis Ltd., Cambridge CB1 9PT, United Kingdom.
SOURCE: INFECTION AND IMMUNITY, (2001 Aug) 69 (8) 4969-79.
Journal code: GO7; 0246127. ISSN: 0019-9567.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200108
ENTRY DATE: Entered STN: 20010827
Last Updated on STN: 20011024
Entered Medline: 20010823

AB Enterotoxigenic Escherichia coli (**ETEC**) is a leading cause of **diarrhea** in travelers to countries where the disease is endemic and causes a major disease burden in the indigenous population, particularly children. We describe here the generation and preclinical characterization of candidate strains of ETEC which are intended to provide the basis of a live attenuated **oral vaccine** to prevent this disease. It has been shown previously that a spontaneously arising toxin-negative variant ETEC strain, E1392/75-2A, could confer 75% protection against challenge when administered to volunteers. Unfortunately this strain induced mild diarrhea in 15% of recipients. To eliminate the unacceptable reactogenicity of strain E1392/75-2A, it was further attenuated by introducing three different combinations of defined deletion mutations into the chromosome. A mouse intranasal model of **immunization** was developed and used to show that all of the strains were immunogenic. Immune responses against **colonization factor antigens** (**CFAs**) were particularly strong when the bacterial inocula were grown on "**CFA** agar," which induces strong expression of these antigens. Two of the strains were selected for a phase I dose escalation safety study with healthy adult volunteers. Freshly grown organisms were harvested from **CFA** agar plates and administered to volunteers as a suspension containing from 5 x 10(7) to 5 x 10(9) CFU. The **vaccine** was well tolerated at all doses and induced significant immune responses in all recipients at the highest dose of either strain. The results provide the basis for further clinical evaluation of these **vaccine** candidates.

L16 ANSWER 3 OF 35 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2002:223218 BIOSIS
DOCUMENT NUMBER: PREV200200223218
TITLE: Comparative safety and immunogenicity of two attenuated enterotoxigenic Escherichia coli (ETEC) **vaccines** in healthy adult volunteers.
AUTHOR(S): Bourgeois, A. L. (1); McKenzie, R. (1); Engstrom, F. (1); Hall, E.; Maples, P. (1); Chang, H. S. (1); Gomes, J. (1); Kyle, J. (1); Turner, A. K.; Darsley, M.; Lee, C.; Bedford, P.; Shimko, J. (1); Sack, D. A.
CORPORATE SOURCE: (1) Vaccine Testing Unit, Dept. Intl. Hlt., Johns Hopkins Univ., Baltimore, MD USA
SOURCE: Abstracts of the General Meeting of the American Society for Microbiology, (2001) Vol. 101, pp. 344. http://www.asmusa.org/mtgsrc/generalmeeting.htm. print.
Meeting Info.: 101st General Meeting of the American Society for Microbiology Orlando, FL, USA May 20-24, 2001
ISSN: 1060-2011.
DOCUMENT TYPE: Conference
LANGUAGE: English

AB **ETEC** remains a serious cause of **diarrhea** among children in developing countries and international travelers. Based

on field and challenge studies, **vaccination** is considered a feasible option for disease prevention. In a previous open-label, inpatient trial, the safety and optimal dosage for two prototype **vaccines** were determined. Both prototypes were prepared from an ETEC strain (E1392/75-2A) expressing **colonization factor antigen** II (**CFA**/II) but not **LT** or ST toxins. The constructs were made by deletion of specific gene combinations from the E1392/75-2A parent. These included aroC and ompR (PTL-002), and aroC, ompC and ompF (PTL-003). In the present study, these constructs were further evaluated for safety and immunogenicity in a randomized, double-blind, placebo-controlled trial using a cross-over design. Both **vaccines** were given **orally** (2X109 cfu/dose) and single (n=19) and two-dose (days 0 and 10) (n=21) **immunization** regimens were compared. Post-dosing general and GI symptoms were assessed by review of diary cards. Induction of **vaccine**-specific mucosal and systemic immune responses were assessed by measurement of anti-**CFA**/II IgA-antibody secreting cells (IgA-ASC) in peripheral blood, as well as serum (IgA and IgG) and fecal (IgA) antibody levels. Although both constructs were well tolerated, PTL-003 exhibited superior immunogenicity and more sustained intestinal colonization. PTL-003 was more effective than PTL-002 in inducing anti-**CFA**/II IgA-ASC (90% vs. 55% responders, $p<0.02$) and serum IgA (35% vs. 0 responders; $p<0.01$) responses. Response profiles for these two immunological parameters were comparable in volunteers given one or two doses of PTL-003. Anti-**CFA**/II serum IgG and fecal IgA responses after **vaccination** followed similar construct-specific trends. In addition, volunteers given PTL-003 had more positive stool cultures post-dosing (4.6 vs. 2.1) than those given PTL-002. Based on the greater immunogenicity and more defined attenuation of the PTL-003 construct, this candidate has been selected for further development as a **vaccine**.

L16 ANSWER 4 OF 35 MEDLINE DUPLICATE 3
ACCESSION NUMBER: 2001464192 MEDLINE
DOCUMENT NUMBER: 21399124 PubMed ID: 11508385
TITLE: Toxins and **colonization factor antigens** of enterotoxigenic Escherichia coli among residents of Jakarta, Indonesia.
AUTHOR: Oyofo B A; Subekti D S; Svennerholm A M; Machpud N N; Tjaniadi P; Komalarini T S; Setiawan B; Campbell J R; Corwin A L; Lesmana M
CORPORATE SOURCE: United States Naval Medical Research Unit No. 2, Jakarta, Indonesia.
SOURCE: AMERICAN JOURNAL OF TROPICAL MEDICINE AND HYGIENE, (2001 Aug) 65 (2) 120-4.
Journal code: 3ZQ; 0370507. ISSN: 0002-9637.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200109
ENTRY DATE: Entered STN: 20010820
Last Updated on STN: 20010910
Entered Medline: 20010906

AB Infection caused by enterotoxigenic Escherichia coli (ETEC) poses a serious health problem among children and adults in developing

countries. Colonization of the small intestinal mucosa by ETEC strains is mediated by antigenically specific fimbriae, also known as **colonization factor antigens** (**CFA**). The significance of this study arises from reports that active and passive **immunization** with ETEC strains harboring **CFAs** has previously been shown to induce protective immunity against diarrhea in animal models. The aim of this study was to determine toxin-associated **CFAs** of **ETEC** isolated from a **diarrheal** disease case-control study in Jakarta, Indonesia. Thirteen hundred and twenty-three diarrheic and control patients with lactose-fermenting colonies were screened by ganglioside GM1-enzyme-linked immunosorbent assay (GM1-ELISA) for **heat-labile** (**LT**) and heat-stable (ST) toxins. Two hundred and forty-six (19%) ETEC isolates identified by GM1-ELISA for the **LT**/ST toxins were screened for **CFAs** by Dot blot assay using monoclonal antibodies against **CFA**/I, II, and IV and against the putative colonization antigens (PCF) PCFO159, PCFO166, CS7, and CS17. Of the 246 ETEC isolates, 177 (72%) elaborated ST, 56 (23%) produced **LT**, while 13 (5%) elicited both the ST and **LT** toxins. **CFA** testing of the 246 ETEC isolates showed that 21 (8%) expressed **CFA** /I, 3 (1%) exhibited **CFA**/II, 14 (6%) elaborated **CFA**/IV, while 7 (3%) expressed PCFO159 and PCFO159 plus CS5. No **CFAs** or PCFs could be associated with 201 (82%) of the ETEC strains. This report documents the types of **CFAs** associated with ETEC strains in Jakarta, Indonesia. These data may help current research efforts on the development of **CFA** -based **vaccines** for humans against ETEC and provide additional information for future ETEC **vaccine** trials in Southeast Asia.

L16 ANSWER 5 OF 35 WPIDS (C) 2002 THOMSON DERWENT DUPLICATE 4
ACCESSION NUMBER: 2000-442539 [38] WPIDS
DOC. NO. CPI: C2000-134660
TITLE: New **oral vaccine** against **enterotoxigenic** Escherichia **coli** which cause **diarrhea** comprising **colonization factor antigens.**
DERWENT CLASS: B04 D16
INVENTOR(S): ASKELOEF, P; BJARE, U; CARLIN, N
PATENT ASSIGNEE(S): (SBLV-N) SBL VACCIN AB
COUNTRY COUNT: 90
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2000037106	A1	20000629	(200038)*	EN	11
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW					
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW					
SE 9804415	A	20000619	(200042)		
AU 2000030889	A	20000712	(200048)		
SE 515285	C2	20010709	(200141)		

NO 2001002889 A 20010612 (200157)
BR 9916278 A 20010904 (200160)
EP 1140159 A1 20011010 (200167) EN
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
CZ 2001001947 A3 20011212 (200206)
CN 1330552 A 20020109 (200229)
KR 2001101233 A 20011114 (200230)
ZA 2001004362 A 20020327 (200230) 15

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2000037106	A1	WO 1999-SE2306	19991209
SE 9804415	A	SE 1998-4415	19981218
AU 2000030889	A	AU 2000-30889	19991209
SE 515285	C2	SE 1998-4415	19981218
NO 2001002889	A	WO 1999-SE2306	19991209
		NO 2001-2889	20010612
BR 9916278	A	BR 1999-16278	19991209
		WO 1999-SE2306	19991209
EP 1140159	A1	EP 1999-964847	19991209
		WO 1999-SE2306	19991209
CZ 2001001947	A3	WO 1999-SE2306	19991209
		CZ 2001-1947	19991209
CN 1330552	A	CN 1999-814553	19991209
KR 2001101233	A	KR 2001-707484	20010615
ZA 2001004362	A	ZA 2001-4362	20010528

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2000030889	A	Based on	WO 200037106
BR 9916278	A	Based on	WO 200037106
EP 1140159	A1	Based on	WO 200037106
CZ 2001001947	A3	Based on	WO 200037106

PRIORITY APPLN. INFO: SE 1998-4415 19981218
AN 2000-442539 [38] WPIDS
AB WO 200037106 A UPAB: 20000811
NOVELTY - New **oral vaccine** (I) against **enterotoxigenic** Escherichia **coli** causing **diarrhea** in humans is new and comprises a defined amount of at least three types of **colonization factor antigens** on killed E. coli bacteria lacking the gene encoding the **heat labile** (**LT**) enterotoxin with the B-subunit of cholera toxin (CTB) and a vehicle.
DETAILED DESCRIPTION - New **oral vaccine** (I) against **enterotoxigenic** Escherichia **coli** causing **diarrhea** in humans is new and comprises a defined amount of at least three types of **colonization factor antigens** (**CFAs**) e.g. **CFA** I, **CFA** II (CS 1 and CS 2 and CS 3) and **CFA** IV (CS 4, CS 5 and CS 6), on killed E. coli bacteria lacking the gene encoding the **heat labile** (**LT**) enterotoxin, together with a predefined amount of the B-subunit of cholera toxin (CTB) and

a vehicle, which **vaccine** composition is purified from possible heat stable enterotoxin.

ACTIVITY - Antibacterial; Antidiarrheic.

MECHANISM OF ACTION - **Vaccine**.

Formulations were given to 3 randomized groups of travelers: (1) 1 mg recombinant B-subunit of cholera toxin plus 1011 formalin killed ETEC bacteria of five ETEC strains expressing the most common **colonization factor antigens** ;

(2) a B-subunit cholera whole cell **vaccine** containing 1 mg recombinant subunit B cholera toxin and 1011 killed whole cells; and

(3) placebo containing 1011 killed E. coli K12.

The formulations were suspended in 4 ml buffer and each dose of **vaccine** or placebo was given as a drink in 150.cc of a sodium hydrogen carbonate solution. 250 volunteers received one dose of **vaccine** or placebo of whom 246 also received a second dose. 43 volunteers (17%) had mild to moderate gastrointestinal or general symptoms, 13 (16%) in the placebo, 13 (16%) in the cholera **vaccine** group and 17 (20%) in the ETEC **vaccine** group. After the second dose 20 (8%) had symptoms, 6 (7%) in the placebo, 7 (9%) in the cholera **vaccine** group and 7 (8%) in the ETEC **vaccine** group.

USE - The **oral vaccine** is useful against **diarrhea**, especially against **enterotoxigenic** Escherichia **coli** causing **diarrhea** in humans.

Dwg.0/0

L16 ANSWER 6 OF 35 MEDLINE

ACCESSION NUMBER: 2000156955 MEDLINE

DOCUMENT NUMBER: 20156955 PubMed ID: 10689236

TITLE: Double-blind, randomized, placebo controlled pilot study evaluating efficacy and reactogenicity of an **oral** ETEC B-subunit-inactivated whole cell **vaccine** against travelers' diarrhea (preliminary report).

AUTHOR: Wiedermann G; Kollaritsch H; Kundi M; Svennerholm A M; Bjare U

CORPORATE SOURCE: Institute for Specific Prophylaxis and Tropical Medicine, University of Vienna, Austria.

SOURCE: JOURNAL OF TRAVEL MEDICINE, (2000 Jan) 7 (1) 27-9. Journal code: C7W; 9434456. ISSN: 1195-1982.

PUB. COUNTRY: Canada

(CLINICAL TRIAL)

Journal; Article; (JOURNAL ARTICLE)

(RANDOMIZED CONTROLLED TRIAL)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200005

ENTRY DATE: Entered STN: 20000518

Last Updated on STN: 20000518

Entered Medline: 20000510

AB **Diarrhea** caused by **enterotoxigenic** E. **coli** (**ETEC**) is an important health problem in developing countries and in travelers to these areas. In previous trials formulations of ETEC **vaccines** containing the B-subunit of cholera toxin, which is antigenically similar to the **heat labile** enterotoxin of ETEC, and the most

prevalent **colonization factor antigens** of ETEC, were shown to stimulate relevant mucosal immune responses in volunteers from Sweden and Egypt.

L16 ANSWER 7 OF 35 MEDLINE DUPLICATE 5
ACCESSION NUMBER: 1999380315 MEDLINE
DOCUMENT NUMBER: 99380315 PubMed ID: 10449484
TITLE: Phenotypic diversity of enterotoxigenic Escherichia coli strains from a community-based study of pediatric diarrhea in periurban Egypt.
AUTHOR: Peruski L F Jr; Kay B A; El-Yazeed R A; El-Etr S H; Cravioto A; Wierzba T F; Rao M; El-Ghorab N; Shaheen H; Khalil S B; Kamal K; Wasfy M O; Svennerholm A M; Clemens J D; Savarino S J
CORPORATE SOURCE: U.S. Naval Medical Research Unit No. 3, Cairo, Egypt.. boushrah@namru3.navy.mil
CONTRACT NUMBER: Y1-HD-0026-01 (NICHD)
SOURCE: JOURNAL OF CLINICAL MICROBIOLOGY, (1999 Sep) 37 (9) 2974-8.
Journal code: HSH; 7505564. ISSN: 0095-1137.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199909
ENTRY DATE: Entered STN: 19990913
Last Updated on STN: 19990913
Entered Medline: 19990902

AB No past studies of diarrhea in children of the Middle East have examined in detail the phenotypes of enterotoxigenic Escherichia coli (ETEC) strains, which are important pathogens in this setting. During a prospective study conducted from November 1993 to September 1995 with 242 children under 3 years of age with diarrhea living near Alexandria, Egypt, 125 episodes of **diarrhea** were positive for **ETEC**. **ETEC** strains were available for 98 of these episodes, from which 100 ETEC strains were selected and characterized on the basis of enterotoxins, colonization factors (CFs), and O:H serotypes. Of these representative isolates, 57 produced heat-stable toxin (ST) only, 34 produced **heat-labile** toxin (**LT**) only, and 9 produced both **LT** and ST. Twenty-three ETEC strains expressed a CF, with the specific factors being CF antigen IV (**CFA**/IV; 10 of 23; 43%), **CFA**/II (5 of 23; 22%), **CFA**/I (3 of 23; 13%), PCFO166 (3 of 23; 13%), and CS7 (2 of 23; 9%). No ETEC strains appeared to express **CFA**/III, CS17, or PCFO159. Among the 100 ETEC strains, 47 O groups and 20 H groups were represented, with 59 O:H serotypes. The most common O serogroups were O159 (13 strains) and O43 (10 strains). O148 and O21 were each detected in five individual strains, O7 and O56 were each detected in four individual strains, O73, O20, O86, and O114 were each detected in three individual strains, and O23, O78, O91, O103, O128, and O132 were each detected in two individual strains. The most common H serogroups were H4 (16 strains), 12 of which were of serogroup O159; H2 (9 strains), all of which were O43; H18 (6 strains); H30 (6 strains); and H28 (5 strains); strains of the last three H serogroups were all O148. Cumulatively, our results suggest a high degree of clonal diversity of disease-associated ETEC strains in this region. As a low percentage of these strains expressed a CF, it

remains possible that other adhesins for which we either did not assay or that are as yet undiscovered are prevalent in this region. Our findings point out some potential barriers to effective **immunization** against **ETEC diarrhea** in this population and emphasize the need to identify additional protective antigens commonly expressed by ETEC for inclusion in future **vaccine** candidates.

L16 ANSWER 8 OF 35 MEDLINE DUPLICATE 6
ACCESSION NUMBER: 1998298053 MEDLINE
DOCUMENT NUMBER: 98298053 PubMed ID: 9632600
TITLE: Intestinal immune responses to an inactivated **oral** enterotoxigenic Escherichia coli **vaccine** and associated immunoglobulin A responses in blood.
AUTHOR: Ahren C; Jertborn M; Svennerholm A M
CORPORATE SOURCE: Departments of Medical Microbiology and Immunology, Goteborg University, Goteborg, Sweden.
SOURCE: INFECTION AND IMMUNITY, (1998 Jul) 66 (7) 3311-6. Journal code: GO7; 0246127. ISSN: 0019-9567.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199807
ENTRY DATE: Entered STN: 19980716
Last Updated on STN: 19980716
Entered Medline: 19980709

AB An inactivated **oral enterotoxigenic** Escherichia **coli** (**ETEC**) **vaccine** against **ETEC diarrhea** was given to 25 adult Swedish volunteers. The **vaccine** consisted of formalin-killed E. coli bacteria expressing the most common **colonization factor antigens** (**CFAs**), i.e., **CFA**/I, -II, and -IV, and recombinantly produced cholera B subunit (CTB). Immunoglobulin A (IgA) antibody responses in intestinal lavage fluid to CTB and **CFAs** were determined and compared with corresponding responses in stool extracts and serum as well as with IgA antibody-secreting cell (ASC) responses in peripheral blood. Two doses of **vaccine** induced significant IgA responses to the different **CFAs** in lavage fluid in 61 to 87% of the **vaccinees** and in stool in 38 to 81% of them. The most frequent responses were seen against **CFA**/I. The magnitudes of the antibody responses against CTB and **CFA**/I in stool correlated significantly (CTB, $P < 0.01$; **CFA**/I, $P < 0.05$) with those in intestinal lavage. Intestinal lavage responses against **CFAs** were best reflected by the ASC responses, with the sensitivity of the ASC assay being 80 to 85%, followed by stool (sensitivity of 50 to 88%) and serum antibody (sensitivity of 7 to 65%) analyses. CTB-specific immune responses were seen in >90% of the **vaccinees** in all assays.

L16 ANSWER 9 OF 35 MEDLINE DUPLICATE 7
ACCESSION NUMBER: 1998158233 MEDLINE
DOCUMENT NUMBER: 98158233 PubMed ID: 9498468
TITLE: Safety and immunogenicity of an **oral**, killed enterotoxigenic Escherichia coli-cholera toxin B subunit **vaccine** in Egyptian adults.

AUTHOR: Savarino S J; Brown F M; Hall E; Bassily S; Youssef F; Wierzba T; Peruski L; El-Masry N A; Safwat M; Rao M; Jertborn M; Svennerholm A M; Lee Y J; Clemens J D
CORPORATE SOURCE: US Naval Medical Research Unit No. 3, Cairo, Egypt.. savarino@namru3.navy.mil
CONTRACT NUMBER: HD-0026-01 (NICHD)
SOURCE: JOURNAL OF INFECTIOUS DISEASES, (1998 Mar) 177 (3) 796-9.
Journal code: IH3; 0413675. ISSN: 0022-1899.
PUB. COUNTRY: United States
(CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(RANDOMIZED CONTROLLED TRIAL)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199803
ENTRY DATE: Entered STN: 19980407
Last Updated on STN: 19980407
Entered Medline: 19980326

AB Enterotoxigenic Escherichia coli (ETEC) is the leading cause of bacterial diarrhea in young children in developing countries. The safety and immunogenicity of a killed, **oral** ETEC **vaccine** consisting of whole cells plus recombinantly produced cholera toxin B subunit (rCTB) was evaluated in Egypt, which is endemic for **ETEC diarrhea**. Seventy-four healthy Egyptian adults (21-45 years old) were randomized and received two doses of the ETEC/rCTB **vaccine** (E003) or placebo 2 weeks apart. The frequency of adverse events after either dose did not differ by treatment group, and no severe adverse events were reported. After **vaccination**, peripheral blood IgA B cell responses to CTB (100%) and to **vaccine** **colonization factor antigens CFA** /I (94%), CS4 (100%), CS2 (81%), and CS1 (69%) were significantly higher than response rates for the placebo group. These favorable results in Egyptian adults indicate that the ETEC/rCTB **vaccine** is a promising candidate for evaluation in younger age groups in this setting.

L16 ANSWER 10 OF 35 MEDLINE DUPLICATE 8
ACCESSION NUMBER: 97305985 MEDLINE
DOCUMENT NUMBER: 97305985 PubMed ID: 9163453
TITLE: Analysis of incidence of infection with enterotoxigenic Escherichia coli in a prospective cohort study of infant diarrhea in Nicaragua.
AUTHOR: Paniagua M; Espinoza F; Ringman M; Reizenstein E; Svennerholm A M; Hallander H
CORPORATE SOURCE: Department of Microbiology, National Autonomous University (UNAN), Leon, Nicaragua.
SOURCE: JOURNAL OF CLINICAL MICROBIOLOGY, (1997 Jun) 35 (6) 1404-10.
Journal code: HSH; 7505564. ISSN: 0095-1137.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199707
ENTRY DATE: Entered STN: 19970721
Last Updated on STN: 19970721

Entered Medline: 19970710

AB **Diarrheal** episodes with **enterotoxigenic** Escherichia **coli** (**ETEC**) were prospectively monitored during the first 2 years of life in a cohort of 235 infants from Leon, Nicaragua. ETEC was an etiological finding in 38% (310 of 808) of diarrheal episodes and in 19% (277 of 1,472) of samples taken as asymptomatic controls at defined age intervals (P = <0.0001). The majority of diarrheal episodes (80%) occurred before 12 months of age. The major ETEC type was characterized by colonization factor **CFA** I and elaboration of both **heat-labile** enterotoxin and heat-stable enterotoxin (ST). The proportion of E. coli strains with **CFA** I was significantly higher in cases with diarrhea (P = 0.002). The second most prevalent type showed putative colonization factor PCFO166 and production of ST. The prevalence of PCFO166 was approximately 20%, higher than reported before. Children with a first **CFA** I episode contracted a second ETEC **CFA** I infection 24% of the time, compared with 46% for ETEC strains of any subtype. Most of the ETEC episodes were of moderate severity, and only 5% (15 of 310) were characterized as severe. In conclusion, our results give valuable information for the planning of intervention studies using ETEC **vaccines**.

L16 ANSWER 11 OF 35 MEDLINE
ACCESSION NUMBER: 97000072 MEDLINE
DOCUMENT NUMBER: 97000072 PubMed ID: 8843215
TITLE: Colonization factors of enterotoxigenic Escherichia coli isolated from children in north India.
COMMENT: Erratum in: J Infect Dis 1996 Nov;174(5):1142
AUTHOR: Sommerfelt H; Steinsland H; Grewal H M; Viboud G I; Bhandari N; Gaastra W; Svennerholm A M; Bhan M K
CORPORATE SOURCE: Center for International Health, Haukeland Hospital, University of Bergen, Norway.
SOURCE: JOURNAL OF INFECTIOUS DISEASES, (1996 Oct) 174 (4) 768-76.
Journal code: IH3; 0413675. ISSN: 0022-1899.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199611
ENTRY DATE: Entered STN: 19961219
Last Updated on STN: 19980206
Entered Medline: 19961107

AB **Colonization factor antigens** (**CFAs**) mediate attachment of enterotoxigenic Escherichia coli (ETEC) to the intestinal mucosa and induce protective immunity against **ETEC diarrhea**. **ETEC** strains (n = 111) isolated from North Indian children from 1985 to 1989 were examined for **CFAs** and putative colonization factors (PCFs). **CFA**/IV was the most common factor (26%), followed by coli surface antigen 17 (CS17) (19%), **CFA**/I (14%), PCFO166 (7%), and **CFA**/II (5%), while 24% of the isolates were negative for **CFAs** and PCFs. Among the strains producing heat-stable and **heat-labile** toxin (ST+ **LT**+ strains), the STaI gene was strongly associated with the absence of known **CFAs** and PCFs, making the STaI+**LT**+ isolates an interesting target for the identification of

previously undescribed factors. Repetitive sequence--based polymerase chain reaction revealed that the CS17+ strains, although clonally related, represented endemically circulating strains with a diversity greater than that of the **CFA**/I+ strains, which showed a substantial clonal clustering.

L16 ANSWER 12 OF 35 MEDLINE DUPLICATE 9
ACCESSION NUMBER: 96264830 MEDLINE
DOCUMENT NUMBER: 96264830 PubMed ID: 8701589
TITLE: Optimization of the intestinal lavage procedure for determination of intestinal immune responses.
AUTHOR: Ahren C; Andersson K; Wiklund G; Wenneras C; Svennerholm A M
CORPORATE SOURCE: Department of Medical Microbiology and Immunology, Goteberg University, Sweden.
SOURCE: VACCINE, (1995 Dec) 13 (18) 1754-8.
Journal code: X60; 8406899. ISSN: 0264-410X.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199609
ENTRY DATE: Entered STN: 19960912
Last Updated on STN: 19960912
Entered Medline: 19960904

AB Optimal conditions to process, concentrate and store intestinal lavage fluid were studied in samples collected from volunteers before and after **oral immunization** with a prototype **vaccine** against **enterotoxigenic** Escherichia **coli** (**ETEC**) **diarrhoea**. Total IgA and specific IgA antibody titres against enterotoxin and **colonization factor antigen** were determined in 22 lavage samples which were either enzyme-inhibited or heat-inactivated and then subjected to different long-term storage conditions. Samples were analysed within 1 month of collection and also after 3, 6 and 24 months of storage. Total IgA concentrations and specific IgA antibody levels were higher in lavage samples treated with enzyme inhibitors (soybean trypsin inhibitor and phenylmethylsulfonyl fluoride) than in those heat-inactivated. Similarily, concentration of the lavage fluid by freeze-drying was superior to concentration against polyethylene glycol. Specific antibody titres remained elevated after storage for at least 6 months but declined after 2 years in frozen compared with freeze-dried samples.

L16 ANSWER 13 OF 35 MEDLINE DUPLICATE 10
ACCESSION NUMBER: 96021580 MEDLINE
DOCUMENT NUMBER: 96021580 PubMed ID: 7483768
TITLE: Simultaneous expression of **CFA**/I and CS3 **colonization factor antigens** of enterotoxigenic Escherichia coli by delta aroC, delta aroD Salmonella typhi **vaccine** strain CVD 908.
AUTHOR: Giron J A; Xu J G; Gonzalez C R; Hone D; Kaper J B; Levine M M
CORPORATE SOURCE: Center for Vaccine Development, School of Medicine, University of Maryland, Baltimore 21201, USA.
CONTRACT NUMBER: RO1 A129471

SOURCE: VACCINE, (1995 Jul) 13 (10) 939-46.
Journal code: X6O; 8406899. ISSN: 0264-410X.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199512
ENTRY DATE: Entered STN: 19960124
Last Updated on STN: 19960124
Entered Medline: 19951228

AB Among the known colonization factors of enterotoxigenic Escherichia coli (ETEC), **CFA**/I and CS3 (the common antigen in the **CFA**/II family of fimbrial antigens) are two of the most prevalent fimbrial antigens found in clinical isolates but are never expressed by the same wild-type strain. We manipulated the genetic determinants encoding CS3 and **CFA**/I fimbriae so that these two important colonization factors are expressed simultaneously in attenuated Salmonella typhi live **oral vaccine** strain CVD 908, including after growth in liquid medium (**CFA**/I is poorly expressed by wild-type ETEC in broth culture). The recombinant fimbrial structures produced by CVD 908 are morphologically indistinguishable from the CS3 fibrillae and **CFA**/I rod-like fimbriae produced by ETEC, and are recognized by monospecific CS3 and **CFA**/I antibodies. This prototype construct may prove useful in investigating the live vector approach to immunoprophylaxis of **ETEC diarrheal** disease.

L16 ANSWER 14 OF 35 MEDLINE DUPLICATE 11
ACCESSION NUMBER: 94025905 MEDLINE
DOCUMENT NUMBER: 94025905 PubMed ID: 8212839
TITLE: Intestinal antibody response after **oral immunization** with a prototype cholera B subunit-**colonization factor antigen** enterotoxigenic Escherichia coli **vaccine**.
AUTHOR: Ahren C; Wenneras C; Holmgren J; Svennerholm A M
CORPORATE SOURCE: Department of Medical Microbiology and Immunology, University of Goteborg, Sweden.
SOURCE: VACCINE, (1993) 11 (9) 929-34.
Journal code: X6O; 8406899. ISSN: 0264-410X.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199310
ENTRY DATE: Entered STN: 19940117
Last Updated on STN: 19950206
Entered Medline: 19931026

AB A prototype **oral** enterotoxigenic Escherichia coli (ETEC) **vaccine** containing formalin-inactivated whole bacteria expressing **colonization factor antigens** **CFA**/I and **CFA**/II and cholera B subunit (CTB) has been tested for safety and immunogenicity in 20 adult Swedish volunteers. When given in three doses with 2-week intervals the **vaccine** was found to be safe and to give rise to specific IgA antibody responses in intestinal lavage fluid in most of the volunteers (**CFA**/I 82%, **CFA**/II 82% and CTB 91%). The frequencies and magnitudes of these responses, which were

already maximal after two doses, were comparable with those previously found in patients convalescing from severe **ETEC diarrhoea**. All the **vaccinated** volunteers also responded with antitoxin IgA as well as IgG antibodies in serum, whereas the serum antibody responses against the **CFAs** were weaker and mainly of the IgA isotype.

L16 ANSWER 15 OF 35 MEDLINE DUPLICATE 12
ACCESSION NUMBER: 94248437 MEDLINE
DOCUMENT NUMBER: 94248437 PubMed ID: 8190998
TITLE: Molecular characterization of enterotoxigenic Escherichia coli (ETEC) isolated in New Caledonia (value of potential protective antigens in **oral vaccine** candidates).
AUTHOR: Begaud E; Mondet D; Germani Y
CORPORATE SOURCE: Institut Pasteur de Nouvelle-Caledonie, Enteric Pathogens Laboratory, Noumea, New Caledonia.
SOURCE: RESEARCH IN MICROBIOLOGY, (1993 Nov-Dec) 144 (9) 721-8.
Journal code: R6F; 8907468. ISSN: 0923-2508.
PUB. COUNTRY: France
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199406
ENTRY DATE: Entered STN: 19940629
Last Updated on STN: 19940629
Entered Medline: 19940620

AB The role of **enterotoxigenic** Escherichia **coli** (**ETEC**) in childhood **diarrhoea** in New Caledonia was demonstrated in previous epidemiological works. This study was undertaken in order to characterize these strains and to determine whether bacterial components of current **vaccine** candidates (toxin, **colonization factor antigens**, O:H antigens) would be useful in our region. A total of 24 ETEC strains were studied: 5 strains produced **heat-labile** enterotoxin, 17 strains produced heat-stable enterotoxin (9 STp and 8 STh), and 2 strains produced both toxins (1 **LT**/STp/STh and 1 **LT**/STh). E. coli strains were screened for the presence of genes encoding for enterotoxins (DNA dot blot and Southern hybridization assays); results obtained with probes were closely correlated and were in agreement with biological assays. No two ETEC strains possessed similar plasmid profiles, and DNA sequences encoding for enterotoxins were located on plasmids ranging from 58 to 75 MDa. The O:H (O1:H-,O2:H7, O6:H16, O25:H-, O27:H7, O28ab:H9, O52:H10, O64:H5, O70:H-, O78:H12, O88:H25, O99:H6, O101:H-, O126:H12, O166:H30) serotypes are presented (all the strains were typable, but some ETEC serotypes were unusual). By using antisera against **colonization factor antigens** (**CFA**) I and II, results showed that 9 of the 24 ETEC strains expressed **CFA** (2 **CFA**/II and 7 **CFA**/I). These strains possessed high bacterial surface hydrophobicity. Fifteen ETEC did not possess **CFA**; among these, 11 did not exhibit high hydrophobicity or show haemagglutination activity. Four of the 15 **CFA**-negative strains exhibited high hydrophobicity (two O64:H45, one O70:H- and one O88:H25) but no haemagglutination in the presence or absence of mannose.(ABSTRACT TRUNCATED AT 250 WORDS)

L16 ANSWER 16 OF 35 WPIDS (C) 2002 THOMSON DERWENT
ACCESSION NUMBER: 1992-315938 [38] WPIDS
DOC. NO. CPI: C1992-140341
TITLE: **Vaccine** contg. formalin-killed Escherichia coli - expressing **colonisation factor antigens**, for preventing enteric infection and diarrhoea.
DERWENT CLASS: B04 D16
INVENTOR(S): HOLMGREN, J; SVENNERHOLM, A; HOLMGREM, J; SVENNERHOLM, A M
PATENT ASSIGNEE(S): (HOLM-I) HOLMGREN J; (SVEN-I) SVENNERHOLM A; (HOLM-I) HOLMGREM J; (SVEN-I) SVENNERHOLM A M
COUNTRY COUNT: 39
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9214487	A1	19920903	(199238)*	EN	45
RW: AT BE CH DE DK ES FR GB GR IT LU MC NL OA SE					
W: AU BB BG BR CA CS FI HU JP KP KR LK MG MN MW NO PL RO RU SD US					
AU 9213308	A	19920915	(199251)		
NO 9303037	A	19930825	(199347)		
EP 573527	A1	19931215	(199350)	EN	
R: AT BE CH DE DK ES FR GB GR IT LI LU MC NL SE					
FI 9303728	A	19931025	(199402)		
CZ 9301742	A3	19940413	(199422)		
BR 9205677	A	19940517	(199423)		
SK 9300910	A3	19940511	(199429)		
JP 06505730	W	19940630	(199430)		10
HU 67198	T	19950228	(199514)		
AU 663864	B	19951026	(199550)		
RO 109819	B1	19950630	(199613)		
CZ 281556	B6	19961113	(199701)		
HU 213924	B	19971128	(199817)		
EP 573527	B1	19980909	(199840)	EN	
R: AT BE CH DE DK ES FR GB GR IT LI LU MC NL SE					
DE 69226944	E	19981015	(199847)		
ES 2123550	T3	19990116	(199909)		
RU 2127121	C1	19990310	(200023)		
NO 307867	B1	20000613	(200035)		
SK 280919	B6	20000912	(200055)		
KR 221452	B1	19990915	(200107)		
JP 3169608	B2	20010528	(200132)		18
FI 108775	B1	20020328	(200223)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9214487	A1	WO 1992-SE110	19920225
AU 9213308	A	AU 1992-13308	19920225
		WO 1992-SE110	19920225
NO 9303037	A	WO 1992-SE110	19920225
		NO 1993-3037	19930825
EP 573527	A1	EP 1992-906078	19920225
		WO 1992-SE110	19920225

FI 9303728	A	WO 1992-SE110	19920225
		FI 1993-3728	19930825
CZ 9301742	A3	CZ 1993-1742	19920225
BR 9205677	A	BR 1992-5677	19920225
		WO 1992-SE110	19920225
SK 9300910	A3	SK 1993-910	19930825
		WO 1992-SE110	
JP 06505730	W	JP 1992-506105	19920225
		WO 1992-SE110	19920225
HU 67198	T	WO 1992-SE110	19920225
		HU 1993-2410	19920225
AU 663864	B	AU 1992-13308	19920225
RO 109819	B1	WO 1992-SE110	19920225
		RO 1993-1142	19920225
CZ 281556	B6	CZ 1993-1742	19920225
HU 213924	B	WO 1992-SE110	19920225
		HU 1993-2410	19920225
EP 573527	B1	EP 1992-906078	19920225
		WO 1992-SE110	19920225
DE 69226944	E	DE 1992-626944	19920225
		EP 1992-906078	19920225
		WO 1992-SE110	19920225
ES 2123550	T3	EP 1992-906078	19920225
RU 2127121	C1	RU 1993-53899	19920225
NO 307867	B1	WO 1992-SE110	19920225
		NO 1993-3037	19930825
SK 280919	B6	WO 1992-SE110	19920225
		SK 1993-910	19920225
KR 221452	B1	WO 1992-SE110	19920225
		KR 1993-702564	19930826
JP 3169608	B2	JP 1992-506105	19920225
		WO 1992-SE110	19920225
FI 108775	B1	WO 1992-SE110	19920225
		FI 1993-3728	19930825

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9213308	A	Based on	WO 9214487
EP 573527	A1	Based on	WO 9214487
BR 9205677	A	Based on	WO 9214487
JP 06505730	W	Based on	WO 9214487
HU 67198	T	Based on	WO 9214487
AU 663864	B	Previous Publ.	AU 9213308
		Based on	WO 9214487
RO 109819	B1	Based on	WO 9214487
CZ 281556	B6	Previous Publ.	CZ 9301742
HU 213924	B	Previous Publ.	HU 67198
		Based on	WO 9214487
EP 573527	B1	Based on	WO 9214487
DE 69226944	E	Based on	EP 573527
		Based on	WO 9214487
ES 2123550	T3	Based on	EP 573527
NO 307867	B1	Previous Publ.	NO 9303037
SK 280919	B6	Previous Publ.	SK 9300910
JP 3169608	B2	Previous Publ.	JP 06505730
		Based on	WO 9214487

FI 108775 B1 Previous Publ. FI 9303728

PRIORITY APPLN. INFO: SE 1991-556 19910226
AN 1992-315938 [38] WPIDS
AB WO 9214487 A UPAB: 19981021
In a method of producing a **vaccine** against enteric infection in humans caused by enterotoxigenic Escherichia coli (ETEC) at least one E. coli strain, selected from strains above to express a certain type of **colonisation factor antigens** (I), is grown in liq. culture medium allowing high level expression of (I) on the surface of the bacteria to a predetermined density. After harvesting and resuspension of the culture in saline, formalin is added, with slight agitation, to a final concn. of 0.2 M formaldehyde. The mixt. is incubated, with continuous agitation, at 37 deg C for about 2 hrs., then at 4 deg.C for 24-48 hrs. This results in a formalin-killed E. coli strain with preserved antigenic and haemagglutinating properties of (I), which is then mixed with a pharmaceutical excipient and/or diluent to a required concn.

USE/ADVANTAGE - The **vaccine** prevents human enteric infection/**diarrhoea** cuased by **ETEC**. High levels of expression of (I) are produced during fermentor culture conditions, and safe killing of the ETEC strains is combined with preservation and stabilisation of (I). No significant side effects have been observed after **oral** administration of the **vaccine**, and two or three doses stimulated IgA antibody formation in intestinal lavage fluid as well as antibody-secreting cells in the circul
Dwg.0/1

L16 ANSWER 17 OF 35 MEDLINE DUPLICATE 13
ACCESSION NUMBER: 92307879 MEDLINE
DOCUMENT NUMBER: 92307879 PubMed ID: 1612729
TITLE: **Oral** ingestion of egg yolk immunoglobulin from hens **immunized** with an **enterotoxigenic** Escherichia **coli** strain prevents **diarrhea** in rabbits challenged with the same strain.
AUTHOR: O'Farrelly C; Branton D; Wanke C A
CORPORATE SOURCE: Biological Laboratories, Harvard University, Cambridge, Massachusetts 02138.
CONTRACT NUMBER: HL 17411 (NHLBI)
SOURCE: INFECTION AND IMMUNITY, (1992 Jul) 60 (7) 2593-7. Journal code: GO7; 0246127. ISSN: 0019-9567.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199207
ENTRY DATE: Entered STN: 19920807
Last Updated on STN: 19920807
Entered Medline: 19920724
AB White Leghorn hens were **immunized** with enterotoxigenic Escherichia coli B16-4 with **heat-labile** enterotoxin and **colonization factor antigen** I in Freund's adjuvant. Specific antibodies were detected by an enzyme-linked immunosorbent assay in the serum after 8 days and in eggs after 10 days, with levels reaching peaks at 15

and 20 days after the first **immunization**, respectively. The protective effects of the egg yolk antibodies were tested in the rabbit reversible ileal tie model of diarrhea. Five control rabbits developed severe diarrhea within 72 h after inoculation with enterotoxigenic E. coli B16-4. **Oral** ingestion of egg yolks from **immunized** hens for 4 days prior to inoculation protected five rabbits from diarrhea after challenge with the same strain of E. coli. The rabbits showed no adverse effects from the ingestion of the egg yolks. Four rabbits fed control eggs were also afforded some protection in that three rabbits developed mild diarrhea and one rabbit remained entirely well. In vitro experiments showed that immunoglobulin from egg yolks interfered with the binding of E. coli to purified small bowel mucins; immunoglobulin from **immunized** hens reduced binding more than immunoglobulin from nonimmunized hens. These findings indicate that eggs from hens **immunized** with appropriate antigens have potential as a useful source of passive immunity.

L16 ANSWER 18 OF 35 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1992:454114 BIOSIS
DOCUMENT NUMBER: BA94:95514
TITLE: EFFICIENT EXPRESSION OF RECOMBINANT PLASMIDS FOR **COLONIZATION FACTOR ANTIGEN** 1 **CFA**-1 IN ESCHERICHIA-COLI.
AUTHOR(S): ZHANG Z-S; ET AL
CORPORATE SOURCE: INSTITUTE BIOTECHNOLOGY, ACADEMY MILITARY MEDICAL SCIENCES, BEIJING.
SOURCE: CHIN J MICROBIOL IMMUNOL (BEIJING), (1992) 12 (3), 157-161.
CODEN: ZWMZDP. ISSN: 0254-5101.
FILE SEGMENT: BA; OLD
LANGUAGE: Chinese
AB We have constructed the plasmids pZLH42 and pZLH88 which contain the structural and regulatory genes for **colonization factor antigen** 1 (**CFA**/1). pZLH42 and pZLH88 have the same size but the inserting direction of the structural gene is just opposite. The expressing level of **CFA**/1 measured by ELISA was of much difference in different E. coli K12 strains harbouring plasmid pZLH42 or pZLH88. The expression of **CFA**/1 in E. coli RR1 or C600 was two-three times higher than E. coli H10407. The expression levels of E. coli Hb101 and E. coli H10407 were similar. The **CFA**/1 recombinant plasmids in E. coli C600 and HB101 were very stable when cultured in antibiotic-free medium. The plasmids in E. coli RR1 showed instability. After 100 generations when cultured in nonselective medium, 70% of cells lose the plasmids. The rabbit ileal loop test for **LT** toxin activity and suckling mice test for ST toxin activity were negative. So the **CFA**/1 recombinant clone could be a good live **vaccine** candidate for prevention of human **diarrhea** caused by **ETEC** bacteria.

L16 ANSWER 19 OF 35 MEDLINE DUPLICATE 14
ACCESSION NUMBER: 93091262 MEDLINE
DOCUMENT NUMBER: 93091262 PubMed ID: 1457822
TITLE: Development of an irradiated **vaccine** that protects against **enterotoxigenic** Escherichia **coli diarrhoea**.

AUTHOR: Dima V F; Ionescu M D; Dima V S; Popa A; Ionescu P
CORPORATE SOURCE: Cantacuzino Institute, Bucharest, Romania.
SOURCE: ROUMANIAN ARCHIVES OF MICROBIOLOGY AND IMMUNOLOGY, (1992 Jan-Jun) 51 (1-2) 5-16.
Journal code: BAQ; 9204717. ISSN: 0004-0037.
PUB. COUNTRY: Romania
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199301
ENTRY DATE: Entered STN: 19930129
Last Updated on STN: 19960808
Entered Medline: 19930113

AB In the pathogenesis of diarrhoea in man bacteria adhesion to enterocytes is mediated by specific **CFA**/I or **CFA** /II antigens. A perorally administered **vaccine** was prepared from E. coli H10407 (078:H11) by irradiation with electrons with high energy (EHE). Two hours after cimetidine administration rats were **immunized per os** with 5 irradiated **vaccine** doses at 4-day intervals. Seven days after the last **immunization** animals were infected by inoculating 1 x 10(9) germs in the ligated intestinal loop. Reduction of the intestinal secretion by over 50% 18 hours after inoculation was considered an efficient protection marker. The obtained results have proved a significant reduction of the intestinal secretion in **immunized** animals infected with serotypes 078:H11(63 +/- 4%) and 078:H12(59 +/- 5%) as compared to non-**immunized** animals. Experimental induction of the intestinal protection against Escherichia coli enterotoxigenic (ETEC) strains points to the possibility of using this type of irradiated **vaccine** in the prophylaxis of diarrhoea in man.

L16 ANSWER 20 OF 35 WPIDS (C) 2002 THOMSON DERWENT
ACCESSION NUMBER: 1991-171163 [23] WPIDS
DOC. NO. CPI: C1991-074027
TITLE: Prodn. of antibody-fortified dry whey - e.g. useful against **diarrhoea**-causing **entero -toxigenic E coli** bacteria, by **immunising** pregnant ungulate with antigens, etc..
DERWENT CLASS: B04 C03 D13
INVENTOR(S): HASTINGS, D H
PATENT ASSIGNEE(S): (MEDI-N) MEDICIS CORP
COUNTRY COUNT: 1
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
US 5017372	A	19910521	(199123)*		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
US 5017372	A	US 1988-259735	19881019

PRIORITY APPLN. INFO: US 1986-851472 19860414; US 1988-259735

19881019
AN 1991-171163 [23] WPIDS
AB US 5017372 A UPAB: 19930928
A dry whey protein powder (I) fortified with polyclonal antibodies against preselected infections intestinal disease antigens (II) is prepd. by (a) **immunising** a pregnant ungulate with (II) in a non-pathogenic condition; (b) collecting and maintaining the milk from the ungulate after parturition, the milk contg. a higher than normal concn. of antibodies against (II) because of the **immunisation** step; (c) producing unfractionated whey, fortified with naturally occurring polyclonal antibodies against (II), from the milk by removing milk casein; and (d) concentrating and drying the unfractionated whey.

(II) is pref. derived from a **diarrhoea**-causing **enterotoxigenic** Escherichia **coli** bacteria bearing at least one of the **colonisation factor antigens** (**CFA**) and **heat labile** toxins.

USE - (I) may be used both prophylactically and therapeutically against the preselected intestinal disease. @(6pp Dwg.No.0/0)

L16 ANSWER 21 OF 35 MEDLINE DUPLICATE 15
ACCESSION NUMBER: 90324659 MEDLINE
DOCUMENT NUMBER: 90324659 PubMed ID: 1973696
TITLE: Enterotoxins and adhesins of enterotoxigenic Escherichia coli: are they risk factors for acute diarrhea in the community?.
AUTHOR: Lopez-Vidal Y; Calva J J; Trujillo A; Ponce de Leon A; Ramos A; Svennerholm A M; Ruiz-Palacios G M
CORPORATE SOURCE: Department of Infectious Diseases, Instituto Nacional de la Nutricion, Tlalpan, Mexico.
CONTRACT NUMBER: HD-13021 (NICHD)
SOURCE: JOURNAL OF INFECTIOUS DISEASES, (1990 Aug) 162 (2) 442-7.
Journal code: IH3; 0413675. ISSN: 0022-1899.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199008
ENTRY DATE: Entered STN: 19901012
Last Updated on STN: 19950206
Entered Medline: 19900827

AB A cohort of 228 Mexican children less than 5 years old was followed during the enterotoxigenic Escherichia coli(**ETEC**) season. The incidence of **ETEC diarrhea**-associated and asymptomatic infections was determined, and E. coli strains isolated from stool samples were tested for **heat-labile** and heat-stable toxins and for expression of **colonization factor antigens** (**CFA**). Of the children, 61% had at least one ETEC infection. Children with ETEC isolated from stools were more likely to have **diarrhea** than were **ETEC**-free age-matched control children (odds ratio [OR] = 4.5; 95% confidence interval [CI] = 2.9-7.0). Strains carrying **CFA**/IV, **CFA**/I, or **CFA**/II were found in 23%, 18%, and 5% of ETEC infections, respectively. The risk of having diarrhea associated with a **CFA**-expressing versus a **CFA**-negative ETEC strain was the same (age-adjusted OR =

0.8; 95% CI = 0.4-1.6). These data should be considered in the development of a diarrhea **vaccine** containing only **CFAs**.

L16 ANSWER 22 OF 35 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 90106116 EMBASE
DOCUMENT NUMBER: 1990106116
TITLE: **Colonization factor antigens** of human pathogens.
AUTHOR: Evans Jr. D.J.; Evans D.G.
CORPORATE SOURCE: Bacterial Enteropathogen Laboratory, Digestive Disease Section, Veterans Administration Medical Center, Houston, TX, United States
SOURCE: Current Topics in Microbiology and Immunology, (1990) 151/- (129-145).
ISSN: 0070-217X CODEN: CTMIA3
COUNTRY: Germany
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 004 Microbiology
LANGUAGE: English
SUMMARY LANGUAGE: English

AB In this chapter we have cited only a few of the many researchers who have contributed to the current state of knowledge about the ETEC and their significance as a major human health problem. Furthermore, there are volumes of data which could be cited concerning the economic cost of ETEC infection of domestic animals, **CFAs** of these animal-associated ETEC other than K88 and K99, and the important strides of progress which have been made in developing an effective **vaccine** approach to deal with these ETEC. Our basic message is that the **CFAs** are the key to survival of the ETEC in any given population, be it man or animal, and we postulated that an anti-ETEC **vaccine** aimed at the **CFAs**, especially if combined with an antienterotoxin stimulus, will prove eventually to be very successful. In terms of economic feasibility, one must consider the current cost of **ETEC diarrhea** in morbidity and mortality in countries with a high endemicity of **ETEC diarrhea**, not to mention treatment costs, costs to travelers, and the effects of **ETEC diarrhea** on child development and increased susceptibility to the devastating effects of other pathogens. We also postulate that one major benefit which will be derived from studies on the ETEC **CFAs** will be elucidation of the **CFA**(s) of Vibrio cholerae and that this achievement will provide the final step in development of an **oral vaccine** remarkably effective against cholera. Discovery of the new ETEC **CFAs**, or putative **CFAs**, cited here makes it imperative that epidemiologic studies on susceptible populations continue, preferably based on an organised surveillance approach rather than on short-term or retrospective studies. Certainly it would be timely, and hopefully economical, to institute newer, rapid identification techniques such as a battery of gene probes which could account for the known ETEC **CFAs** as well as the adhesive factors of the non-ETEC enteropathogenic E. coli. Finally, it will be interesting to see the evolutionary history of the ETEC **CFAs** unfold as newer techniques such as computer-assisted restriction endonuclease analysis and protein/antigen analysis are put to the task. Here, we suggest that the range of E. coli fimbriae selected for examination be expanded

to include all of the known types of sex pili, i.e., those fimbriae involved in DNA transfer between E. coli cells. These seemingly irrelevant pili may prove to be related, in an ancestral fashion, to the fimbrial/fibrillar **CFAs**. Also, elucidation of the molecular mechanics by which chromosomal and plasmid control mechanisms interact may lead to practical applications, even to completely new approaches to prophylaxis and treatment of diseases caused by pathogenic bacteria which are dependent on plasmid-encoded virulence factors.

L16 ANSWER 23 OF 35 MEDLINE DUPLICATE 16
ACCESSION NUMBER: 89389466 MEDLINE
DOCUMENT NUMBER: 89389466 PubMed ID: 2675484
TITLE: Development of **oral vaccines** against **enterotoxinogenic** Escherichia **coli diarrhoea**.
AUTHOR: Svennerholm A M; Holmgren J; Sack D A
CORPORATE SOURCE: Department of Medical Microbiology, University of Goteborg, Sweden.
SOURCE: VACCINE, (1989 Jun) 7 (3) 196-8. Ref: 14
Journal code: X6O; 8406899. ISSN: 0264-410X.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198910
ENTRY DATE: Entered STN: 19900309
Last Updated on STN: 19900309
Entered Medline: 19891016

AB Even though enterotoxin-producing Escherichia coli (ETEC) is the most important cause of diarrhoea in developing countries and among travellers, no **vaccine** for use in humans is yet available. New knowledge about virulence factors and protective antigens of ETEC, however, suggests that development of a useful **vaccine** may soon become possible. Such a **vaccine** should be given **orally** and ideally evoke both anticolonization and antitoxic immune responses in the gut. An **oral** cholera **vaccine**, containing a component (B subunit) which crossreacts immunologically with the major, **heat-labile** enterotoxin (**LT**) of ETEC, has been shown to afford significant protection against **diarrhoea** caused by **LT**-producing **ETEC**. Promising prototype **oral** ETEC **vaccines** combining B subunit toxoid with inactivated ETEC bacteria expressing the most prevalent **colonization factor antigens** (**CFAs**) have been developed, and work is in progress to find means for adding to this **CFA**-toxoid **vaccine** a component that could also provide immunity against heat-stable enterotoxin.

L16 ANSWER 24 OF 35 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC. DUPLICATE 17
ACCESSION NUMBER: 1989:223827 BIOSIS
DOCUMENT NUMBER: BA87:115444
TITLE: NON-REPLICATING **ORAL** WHOLE CELL **VACCINE** PROTECTIVE AGAINST

ENTEROTOXIGENIC ESCHERICHIA-**COLI**
ETEC DIARRHEA STIMULATION OF ANTI-
CFA CFA-I AND ANTI-ENTEROTOXIN
ANTI-**LT** INTESTINAL IGA AND PROTECTION
AGAINST CHALLENGE WITH ETEC BELONGING TO HETEROLOGOUS
SEROTYPES.

AUTHOR(S): EVANS D G; EVANS D J JR; OPEKUN A R; GRAHAM D Y
CORPORATE SOURCE: VA MED. CENTER, 2002 HOLCOMBE BLVD., HOUSTON, TX 77211, USA.

SOURCE: FEMS (FED EUR MICROBIOL SOC) MICROBIOL IMMUNOL, (1988) 47 (3), 117-126.
CODEN: FMIMEH.
FILE SEGMENT: BA; OLD
LANGUAGE: English

AB An **oral** killed (non-replicating) whole-cell anti-ETEC **vaccine** was prepared by treating enterotoxigenic Escherichia coli strain H-10407 (ST + **LT**+ ; 078:H11:**CFA**/I) with a 100%-lethal amount of colicin E2. Colicin E2 is a potent DNA endonuclease which enters the target bacterial cells without disrupting cellular integrity. Thus the **vaccine** consists of intact cells lacking chromosomal and plasmid DNA but possessing a normal complement of antigens, including **CFA**/I and enterotoxin(s), unaltered by chemical- or heat-treatment. Young healthy volunteers were administered two **oral** doses, one month apart, of approximately 3 .times. 1010 **vaccine** cells. Of 22 **vaccinees**, 17 (77.3%) showed an intestinal anti-**CFA**/I IgA response and 19 (86.4%) showed an increase in intestinal anti-**LT** IgA. Twenty of 22 (90.9%) **vaccinees** had antibody responses to either **CFA**/I, **LT**, or both antigens, demonstrating that colicin E2-treated **CFA**-positive E. coli cells are an efficient vehicle in terms of delivery of antigens to the gut immune system. We previously demonstrated protection of **vaccinees** against challenge with the living homologous ETEC (strain H-10407). In this study, two groups of 8 **vaccinees** were challenged with a **diarrheagenic** dose of virulent ST + **LT** + **ETEC** of heterologous serotype; one group was challenged with a **CFA**/I-positive 063:H- strain and the other group was challenged with a **CFA**/II-positive 06:H16 strain. Approximately 75% efficacy was achieved in both challenge groups. None of the 16 **vaccinees** who had responded to both **CFA**/I and **LT** became ill upon challenge while both of the **vaccinees** who had not responded to either antigen did. That protection against challenge with heterologous ETEC was due to non-specific immunostimulation proved to be unlikely since only 1 of the remaining 6 **vaccinees** showed mild symptoms when challenged with strain H-10407 6 months after **vaccination**. These results indicate that ETEC heterologous with respect to O, H, and **CFA** may share other antigens which contribute to a protective intestinal immune response.

L16 ANSWER 25 OF 35 MEDLINE
ACCESSION NUMBER: 90212270 MEDLINE
DOCUMENT NUMBER: 90212270 PubMed ID: 3078739
TITLE: Non-replicating **oral** whole cell **vaccine** protective against **enterotoxigenic** Escherichia **coli** (**ETEC**) **diarrhea**: stimulation of

anti-**CFA** (**CFA**/I) and
anti-enterotoxin (anti-**LT**) intestinal IgA
and protection against challenge with ETEC belonging
to heterologous serotypes.

AUTHOR: Evans D G; Evans D J Jr; Opekun A R; Graham D Y
CORPORATE SOURCE: Mucosal Immunity Laboratory, Veterans Administration
Medical Center, Houston, Texas 77211.

CONTRACT NUMBER: M01 RR00350 (NCRR)
R22 DK-35369 (NIDDK)
SOURCE: FEMS MICROBIOLOGY IMMUNOLOGY, (1988 Dec) 1 (3)
117-25.
Journal code: AO3; 8901230. ISSN: 0920-8534.
PUB. COUNTRY: Netherlands
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199005
ENTRY DATE: Entered STN: 19900622
Last Updated on STN: 19970203
Entered Medline: 19900514

AB An **oral** killed (non-replicating) whole-cell anti-ETEC **vaccine** was prepared by treating enterotoxigenic Escherichia coli strain H-10407 (ST + **LT** +; 078: H11: **CFA**/I) with a 100%-lethal amount of colicin E2. Colicin E2 is a potent DNA endonuclease which enters the target bacterial cells without disrupting cellular integrity. Thus the **vaccine** consists of intact cells lacking chromosomal and plasmid DNA but possessing a normal complement of antigens, including **CFA**/I and enterotoxin(s), unaltered by chemical- or heat-treatment. Young healthy volunteers were administered two **oral** doses, one month apart, of approximately 3 x 10(10) **vaccine** cells. Of 22 **vaccinees**, 17 (77.3%) showed an intestinal anti-**CFA**/I IgA response and 19 (86.4%) showed an increase in intestinal anti-**LT** IgA. Twenty of 22 (90.9%) **vaccinees** had antibody responses to either **CFA**/I, **LT**, or both antigens, demonstrating that colicin E2-treated **CFA**-positive E. coli cells are an efficient vehicle in terms of delivery of antigens to the gut immune system. We previously demonstrated protection of **vaccinees** against challenge with the living homologous ETEC (strain H-10407). In this study, two groups of 8 **vaccinees** were challenged with a **diarrheagenic** dose of virulent ST + **LT** + **ETEC** of heterologous serotype; one group was challenged with a **CFA**/I-positive 063: H- strain and the other group was challenged with a **CFA**/II-positive 06: H16 strain. Approximately 75% efficacy was achieved in both challenge groups. None of the 16 **vaccinees** who had responded to both **CFA**/I and **LT** became ill upon challenge while both of the **vaccinees** who had not responded to either antigen did.(ABSTRACT TRUNCATED AT 250 WORDS)

L16 ANSWER 26 OF 35 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
DUPLICATE 18

ACCESSION NUMBER: 1989:268509 BIOSIS
DOCUMENT NUMBER: BA88:4591

TITLE: IMMUNOPROTECTIVE **ORAL** WHOLE CELL **VACCINE** FOR **ENTEROTOXIGENIC** ESCHERICHIA-**COLI DIARRHEA**

PREPARED BY IN SITU DESTRUCTION OF CHROMOSOMAL AND PLASMID DNA WITH COLICIN E2.

AUTHOR(S): EVANS D J JR; EVANS D G; OPEKUN A R; GRAHAM D Y
CORPORATE SOURCE: VA MED. CENTER, 2002 HOLCOMBE BLVD., HOUSTON, TX 77211, USA.

SOURCE: FEMS (FED EUR MICROBIOL SOC) MICROBIOL IMMUNOL, (1988) 47 (1), 9-18.
CODEN: FMIMEH.
FILE SEGMENT: BA; OLD
LANGUAGE: English

AB **Vaccine** regimens which mimic actual infection with bacterial enteropathogen should offer the best opportunity for successful long-term immunopretection against **diarrheal** disease caused by **enterotoxigenic** Escherichia **coli** (ETEC) or Vibrio cholerae. Based on this principle, we designed and tested on **oral** whole cell anti-ETEC **vaccine** consisting of intact cells of ETEC strain H-10407 (ST+**LT**+; O78 : H11 : **CFA**/I) which were rendered incapable of replication by treatment with a potent DNA endonuclease, colicin E2. Young healthy volunteers were administered two **oral** doses of either placebo or approx. 3 .times. 1010 **vaccine** cells. In a double-blind study, 9 of 10 **vaccinees** responded with an increase in **CFA**/I-specific intestinal IgA antibody, determined as percent of total IgA. Challenge with virulent strain H-10407 (5 .times. 109 living cells) produced diarrhea in 8 of 9 (89%) of the placebo-treated volunteers and in 2 of 10 (20%) of the **vaccinees**. Thus, the colicin E2-killed whole cell **vaccine** afforded both a significant intestinal immune response and significant protection against challenge with the virulent organism. The data presented here suggest that for this **vaccine** preparation on intestinal anti-**CFA**/I IgA response is a good indicator of a protective immune response, which most likely involves antibody responses to a number of antigenes in addition to **CFA**/I. We conclude that the colicin E2 method for preparing an **oral** anti-ETEC **vaccine** merits further study and that this method may also be applicable to other enteropathogens.

L16 ANSWER 27 OF 35 MEDLINE

ACCESSION NUMBER: 90180994 MEDLINE
DOCUMENT NUMBER: 90180994 PubMed ID: 3078575

TITLE: Immunoprotective **oral** whole cell **vaccine** for **enterotoxigenic** Escherichia **coli diarrhea** prepared by in situ destruction of chromosomal and plasmid DNA with colicin E2.

AUTHOR: Evans D J Jr; Evans D G; Opekun A R; Graham D Y
CORPORATE SOURCE: Mucosal Immunity Laboratory, Veterans Administration Medical Center, Houston, Texas 77211.

CONTRACT NUMBER: M01 RR00350 (NCRR)
R22 AM35369 (NIADDK)
S07RR05425 (NCRR)
SOURCE: FEMS MICROBIOLOGY IMMUNOLOGY, (1988 Jan) 1 (1) 9-18.
Journal code: AO3; 8901230. ISSN: 0920-8534.
PUB. COUNTRY: Netherlands
(CLINICAL TRIAL)
(CONTROLLED CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199004
ENTRY DATE: Entered STN: 19900601
Last Updated on STN: 19970203
Entered Medline: 19900426

AB **Vaccine** regimens which mimic actual infection with bacterial enteropathogens should offer the best opportunity for successful long-term immunoprotection against **diarrheal** disease caused by **enterotoxigenic** Escherichia **coli** (ETEC) or Vibrio cholerae. Based on this principle, we designed and tested an **oral** whole cell anti-ETEC **vaccine** consisting of intact cells of ETEC strain H-10407 (ST+**LT**+; O78:H11:**CFA**/I) which were rendered incapable of replication by treatment with a potent DNA endonuclease, colicin E2. Young healthy volunteers were administered two **oral** doses of either placebo or approx. 3 X 10(10) **vaccine** cells. In a double-blind study, 9 of 10 **vaccinees** responded with an increase in **CFA**/I-specific intestinal IgA antibody, determined as percent of total IgA. Challenge with virulent strain H-10407 (5 X 10(9) living cells) produced diarrhea in 8 of 9 (89%) of the placebo-treated volunteers and in 2 of 10 (20%) of the **vaccinees**. Thus, the colicin E2-killed whole cell **vaccine** afforded both a significant intestinal immune response and significant protection against challenge with the virulent organism. The data presented here suggest that for this **vaccine** preparation an intestinal anti-**CFA**/I IgA response is a good indicator of a protective immune response, which most likely involves antibody responses to a number of antigens in addition to **CFA**/I. We conclude that the colicin E2 method for preparing an **oral** anti-ETEC **vaccine** merits further study and that this method may also be applicable to other enteropathogens.

L16 ANSWER 28 OF 35 MEDLINE DUPLICATE 19
ACCESSION NUMBER: 86007035 MEDLINE
DOCUMENT NUMBER: 86007035 PubMed ID: 2864313
TITLE: Experimental **enterotoxin**-induced Escherichia **coli diarrhea** and protection induced by previous infection with bacteria of the same adhesin or enterotoxin type.
AUTHOR: Ahren C M; Svennerholm A M
SOURCE: INFECTION AND IMMUNITY, (1985 Oct) 50 (1) 255-61.
Journal code: GO7; 0246127. ISSN: 0019-9567.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198510
ENTRY DATE: Entered STN: 19900321
Last Updated on STN: 19950206
Entered Medline: 19851029

AB The diarrheal response to an initial and a second infection with Escherichia coli expressing various enterotoxins (the heat-stable toxin [ST] alone or in combination with the **heat-labile** toxin [**LT**]) and **colonization factor antigens** (**CFA**/I, **CFA**/II, or E8775-type) was studied in the reversible tie adult rabbit

diarrhea model. An initial infection with high doses (1 X 10(10) to 5 X 10(11) bacteria) of the various strains regularly induced diarrhea which was usually self-limiting (only 7 of 85 animals died). The diarrheal response to equally effective doses of different strains producing both ST and **LT** (ST/**LT**) did not differ significantly with serotype or **colonization factor antigen**. ST/**LT**-producing strains appeared to induce severe disease more regularly than ST-producing strains carrying the same adhesin. Previous infection with **CFA**/I-carrying, ST/**LT**-producing E. coli protected all animals reinfected with an otherwise highly diarrheogenic dose of the same strain as well as against challenge with a **CFA**/I-carrying, ST/**LT**-producing strain with different O-, K-, and H-antigens. Fecal excretion of bacteria was also significantly reduced in the protected animals, although not completely eliminated. When only one of the two antigens, **CFA**/I and **LT**, was shared by the **immunizing** and rechallenge strains, partial protection was evident consistent with independent antibacterial (anti-**CFA**) and antitoxic (anti-**LT**) immune mechanisms. **Oral immunization** with purified **CFA**/I significantly reduced fluid secretion in intestinal loops infected with **CFA**/I-carrying enterotoxigenic bacteria.

L16 ANSWER 29 OF 35 MEDLINE DUPLICATE 20
ACCESSION NUMBER: 83159807 MEDLINE
DOCUMENT NUMBER: 83159807 PubMed ID: 6131869
TITLE: **Colonization factor antigens** I and II and type 1 somatic pili in enterotoxigenic Escherichia coli: relation to enterotoxin type.
AUTHOR: Levine M M; Ristaino P; Sack R B; Kaper J B; Orskov F; Orskov I
CONTRACT NUMBER: NO1AI12666 (NIAID)
NO1AI42553 (NIAID)
SOURCE: INFECTION AND IMMUNITY, (1983 Feb) 39 (2) 889-97.
Journal code: GO7; 0246127. ISSN: 0019-9567.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198305
ENTRY DATE: Entered STN: 19900318
Last Updated on STN: 19970203
Entered Medline: 19830505

AB Enterotoxigenic Escherichia coli (ETEC) isolates from 36 persons with acute traveler's diarrhea from whom no other pathogens were recovered were tested (after no more than three subcultures) for the presence of **colonization factor antigens** I and II (**CFA**/I and **CFA**/II) and type 1 somatic pili. **CFA**/I or **CFA**/II was identified in 7 of 10 strains with **heat-labile** and heat-stable enterotoxins (**LT**+/ST+), but in only 2 of 12 **LT**-/ST+ (P less than 0.05) and 0 of 14 **LT**+/ST- (P less than 0.02) strains. **CFA** pili were not found among 74 non-enterotoxigenic E. coli strains. Type 1 somatic pili were demonstrable in 42% of the 36 ETEC and in 49% of the 74 non-enterotoxigenic E. coli isolates. The nine ETEC isolates bearing

a **CFA** were serially subcultured on 10 consecutive days and retested for **CFA** and toxin. After five subcultures only one strain had lost a **CFA**, but after 10 passages three strains were negative: two lost **CFA**/I and one lost **CFA**/II. The strain that lost **CFA**/II became negative for both **LT** and ST as well and was found to lack a 48- and a 60-megadalton plasmid. The two strains that lost **CFA**/I also became negative for ST, but plasmid analysis revealed no plasmid loss. Disappearance of the **CFA**/I phenotype without loss of a plasmid can be explained by phase variation, as exhibited by type 1 somatic pili, or by rearrangement of base sequences in the **CFA**/I plasmid genome. If purified pili **vaccines** are to provide broad-spectrum protection against **ETEC diarrhea**, the search must be intensified to identify the antigens responsible for adhesion to intestinal mucosa in the many ETEC strains that lack **CFA**/I and **CFA**/II.

L16 ANSWER 30 OF 35 MEDLINE DUPLICATE 21
ACCESSION NUMBER: 83079238 MEDLINE
DOCUMENT NUMBER: 83079238 PubMed ID: 6756908
TITLE: Correlation between intestinal immune response to **colonization factor antigen** /I and acquired resistance to **enterotoxigenic** Escherichia **coli diarrhea** in an adult rabbit model.
AUTHOR: Evans D G; de la Cabada F J; Evans D J Jr
SOURCE: EUROPEAN JOURNAL OF CLINICAL MICROBIOLOGY, (1982 Jun) 1 (3) 178-85.
Journal code: EMY; 8219582. ISSN: 0722-2211.
PUB. COUNTRY: GERMANY, WEST: Germany, Federal Republic of
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198302
ENTRY DATE: Entered STN: 19900317
Last Updated on STN: 19900317
Entered Medline: 19830214

AB Immunoprotection against diarrhea caused by **colonization factor antigen**/I (**CFA**/I)-positive, human-associated, enterotoxigenic Escherichia coli was investigated using the adult rabbit intestinal temporary ligation technique. An **oral** dose of 1 X 10(8) viable cells of enterotoxigenic Escherichia coli strain H-10407 (078:H11:**CFA**/I) produced diarrhea in all animals challenged. Rabbits allowed to survive this challenge dose were re-challenged approximately six weeks later with the result that four of seven (57%) did not develop diarrhea. Peroral **immunization** of rabbits with purified **CFA** /I elicited protection against challenge with strain H-10407; this protection was dose-related and **CFA**/I-specific. Immunoprotection did not correlate with a systemic antibody response. **CFA**/I produced a relatively poor immune response in terms of the number of IgM- and IgG-producing cells in the lamina propria of the animals but did elicit a vigorous increase in the number of intestinal IgA- and anti-**CFA**/I-producing cells. There was a highly significant inverse relationship between the number of IgA- and anti-**CFA**/I-producing cells in the lamina propria of the rabbits and the diarrhea response to the

challenge strain H-10407 (correlation coefficients of -0.616 and -0.678 respectively). It is concluded that anti-**CFA**/I antibody, probably of the IgA class, is the major immune response to **orally** administered **CFA**/I and that this response is highly immunoprotective.

L16 ANSWER 31 OF 35 MEDLINE
ACCESSION NUMBER: 83041096 MEDLINE
DOCUMENT NUMBER: 83041096 PubMed ID: 6127806
TITLE: Reactogenicity, immunogenicity and efficacy studies of Escherichia coli type 1 somatic pili parenteral **vaccine** in man.
AUTHOR: Levine M M; Black R E; Brinton C C Jr; Clements M L; Fusco P; Hughes T P; O'Donnell S; Robins-Browne R; Wood S; Young C R
SOURCE: SCANDINAVIAN JOURNAL OF INFECTIOUS DISEASES. SUPPLEMENTUM, (1982) 33 83-95.
Journal code: UCY; 0251025. ISSN: 0300-8878.
PUB. COUNTRY: Sweden
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198212
ENTRY DATE: Entered STN: 19900317
Last Updated on STN: 19950206
Entered Medline: 19821221

AB Purified type 1 somatic pili from enterotoxigenic Escherichia coli (ETEC) strain H10407 (O78:H11) was evaluated as a parenteral **immunizing** agent in the hope that this antigen might enhance a contemplated polyvalent pilus **vaccine**. Intramuscular inoculation with 45, 90, 900 or 1 800 mcg of pili **vaccine** was tolerated without incident in 82 volunteers. Six of 15 persons who received a 28 day booster of 1 800 mcg developed local reactions while none of 52 persons receiving 180 or 450 mcg boosters evinced such reactions. Pili **vaccine** did not significantly alter intestinal transit time, absorptive capacity or the prevalence of colonic E. coli bearing type 1 somatic pili of the H10407 antigenic variety. All **vaccinees** developed significant rises in circulating IgG antibody to type 1 somatic pili, the magnitude of the response being directly proportioned to the **vaccine** dose. None of the **vaccinees** had significant rises to **CFA** I or II pili nor to **heat-labile** enterotoxin. However, many had rises in O antibody, particularly among those inoculated with 1 800 mcg. Three challenge studies were carried out with E. coli H10407 to assess **vaccine** efficacy. In the initial study the **vaccinees** were either protected against diarrhea (2 of 6 **vaccinees** versus 7/7 of controls) or had milder disease than the controls. In two subsequent challenges with H10407 significant protection was not seen. It was not clear whether protection exhibited by the **vaccinee** group in the first challenge was due to O antibody, pili antibody, or both acting synergistically. To clarify this, a group of the **immunized** volunteers were challenged with ETEC strain B7A which is a different serotype (O148:H28) lacks **CFA**/I or II pili, but possesses type 1 somatic pili antigenically distantly related to those of H10407. Attack rates and severity of illness were similar in both **vaccinee** and control groups. While most volunteers challenged with E. coli H10407 developed significant

rises in circulating antibody to **CFA**/I, **LT** and O antigen, none had rises to type 1 somatic pili. It is unclear if this is due to immune tolerance to this antigen when encountered enterally or whether these pili are not present in vivo in **ETEC** initiating **diarrhea** in the proximal small intestine. In summary, parenterally inoculated type 1 somatic pili were safe and highly immunogenic in man but did not consistently induce protection. Further studies are planned to clarify the role of antibody to type 1 somatic pili in mediating protection.

L16 ANSWER 32 OF 35 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 83021686 EMBASE
DOCUMENT NUMBER: 1983021686
TITLE: Reactogenicity, immunogenicity and efficacy studies of Escherichia coli type 1 somatic pili parenteral **vaccine** in man.
AUTHOR: Levine M.M.; Black R.E.; Brinton Jr. C.C.; et al.
CORPORATE SOURCE: Cent. Vaccine Dev., Univ. Maryland, Sch. Med., Baltimore, MD, United States
SOURCE: Scandinavian Journal of Infectious Diseases, (1982) 14/Suppl.33 (83-95).
CODEN: SJIDB7
COUNTRY: Sweden
DOCUMENT TYPE: Journal
FILE SEGMENT: 026 Immunology, Serology and Transplantation
004 Microbiology
LANGUAGE: English

AB Purified type 1 somatic pili from enterotoxigenic Escherichia coli (ETEC) strain H10407 (078:H11) was evaluated as a parenteral **immunizing** agent in the hope that this antigen might enhance a contemplated polyvalent pilus **vaccine**. Intramuscular inoculation with 45, 90, 900 or 1800 mcg of pili **vaccine** was tolerated without incident in 82 volunteers. Six of 15 persons who received a 28 day booster of 1800 mcg developed local reactions while none of 52 persons receiving 180 or 450 mcg boosters evinced such reactions. Pili **vaccine** did not significantly alter intestinal transit time, absorptive capacity or the prevalence of colonic E. coli bearing type 1 somatic pili of the H10407 antigenic variety. All **vaccinees** developed significant rises in circulating IgG antibody to type 1 somatic pili, the magnitude of the response being directly proportioned to the **vaccine** dose. None of the **vaccinees** had significant rises to **CFA** I or II pili nor to **heat-labile** enterotoxin. However, many had risen in O antibody, particularly among those inoculated with 1800 mcg. Three challenge studies were carried out with E. coli H10407 to assess **vaccine** efficacy. In the initial study the **vaccinees** were either protected against diarrhea (2 of 6 **vaccinees** versus 7/7 of controls) or had milder disease than the controls. In two subsequent challenges with H10407 significant protection was not seen. It was not clear whether protection exhibited by the **vaccine** group in the first challenge was due to O antibody, pili antibody, or both acting synergistically. To clarify this, a group of the **immunized** volunteers were challenged with ETEC strain B7A which is a different serotype (O148:H28) lacks **CFA**/I or II pili, but possesses type 1 somatic pili antigenically distantly relatd to those of H10407. Attack rates and severity of illness were similar in both **vaccinee** and control groups. While most

volunteers challenged with E. coli H10407 developed significant rises in circulating antibody to **CFA**/I, **LT** and O antigen, none had risen to type 1 somatic pili. It is unclear if this is due to immune tolerance to this antigen when encountered enterally or whether these pili are not present in vivo in **ETEC** initiating **diarrhea** in the proximal small intestine. In summary, parenterally inoculated type 1 somatic pili were safe and highly immunogenic in man but did not consistently induce protection. Further studies are planned to clarify the role of antibody to type 1 somatic pili in mediating protection.

L16 ANSWER 33 OF 35 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
DUPLICATE 22
ACCESSION NUMBER: 1982:54932 BIOSIS
DOCUMENT NUMBER: BR22:54932
TITLE: IMMUNO PROTEIN AGAINST **ENTERO TOXIGENIC** ESCHERICHIA-**COLI DIARRHEA** IN RABBITS BY PER **ORAL** ADMINISTRATION OF PURIFIED **COLONIZATION FACTOR ANTIGEN**.
AUTHOR(S): DE LA CABADA F; EVANS D G; EVANS D J JR
CORPORATE SOURCE: PROGRAM INFECTIOUS DISEASES, UNIV. TEXAS MED. SCHOOL AT HOUSTON, HOUSTON, TX 77030.
SOURCE: FEMS Microbiol. Lett., (1981) 11 (4), 303-308.
CODEN: FMLED7. ISSN: 0378-1097.
FILE SEGMENT: BR; OLD
LANGUAGE: English

L16 ANSWER 34 OF 35 MEDLINE
ACCESSION NUMBER: 81260042 MEDLINE
DOCUMENT NUMBER: 81260042 PubMed ID: 6114818
TITLE: Adhesion of enterotoxigenic Escherichia coli in humans and animals.
AUTHOR: Levine M M
CONTRACT NUMBER: NO1A142553
SOURCE: CIBA FOUNDATION SYMPOSIUM, (1981) 80 142-60. Ref: 25
Journal code: D7X; 0356636. ISSN: 0300-5208.
PUB. COUNTRY: Netherlands
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198110
ENTRY DATE: Entered STN: 19900316
Last Updated on STN: 19950206
Entered Medline: 19811014

AB **Enterotoxigenic** Escherichia **coli** (**ETEC**), an important cause of **diarrhoea** in humans and animal, require accessory virulence properties in addition to enterotoxin to manifest virulence. Several classes of pili (hair-like protein surface organelles) promote adhesion of ETEC to small intestinal mucosa. Antibody directed against adhesion pili interferes with colonization of the small intestine and prevents disease. This paper reviews studies with purified K88, K99 and 987 type pili used as parenteral **vaccines** in pregnant pigs and cattle. Infant animals suckled on **immunized** mothers were significantly protected against fatal disease. **Colonization factor antigen** (**CFA**) I and II pili, and

type 1 somatic pili, promote adhesion of human ETEC pathogens to epithelial cells in vitro and are generally recognized as accessory virulence factors. **CFA**/I and II were found in only 25% of 36 human ETEC infections; positive strains were usually **LT** +/ST+ (**LT: heat-labile**; ST: heat-stable). Strains lacking **CFA**/I and II are virulent; other factors must be responsible for adhesion in such strains. While none of 14 **LT**+/ST- strains elaborated **CFA** /I or II, 10 (71%) possessed type 1 somatic pili. An initial **ETEC diarrhoeal** infection in volunteers stimulated protective immunity against diarrhoea on re-challenge with the same strain. Despite clinical protection healthy "veterans" excreted the ETEC strain to the same degree as ill controls. Thus the mechanisms of immunity was not bactericidal. Disease-induced **LT** antitoxic immunity failed to protect volunteers against challenge with a heterologous (**LT**+/ST-) strain. One explanation of these observations is that the mechanism of protection was anti-adhesive with antibody directed against adhesive factors on the bacterial surface preventing attachment of bacteria to receptors on small intestinal mucosal cells. Immunoprophylaxis against ETEC in humans with purified pili **vaccines** appears feasible.

L16 ANSWER 35 OF 35 MEDLINE DUPLICATE 23
ACCESSION NUMBER: 80026449 MEDLINE
DOCUMENT NUMBER: 80026449 PubMed ID: 39896
TITLE: Purification and characterization of the **CFA** /I antigen of enterotoxigenic Escherichia coli.
AUTHOR: Evans D G; Evans D J Jr; Clegg S; Pauley J A
SOURCE: INFECTION AND IMMUNITY, (1979 Aug) 25 (2) 738-48. Journal code: GO7; 0246127. ISSN: 0019-9567.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 197912
ENTRY DATE: Entered STN: 19900315
Last Updated on STN: 19950206
Entered Medline: 19791220

AB The fimbral **colonization factor antigen** **CFA**/I of enterotoxigenic Escherichia coli was purified and characterized. The initial purification step was release of these fimbriae from the bacterial cells by homogenization with a Waring blender. Common fimbriae and flagellar antigen were avoided by careful control of growth conditions and the use of a nonmotile (H-) mutant of the prototype strain H-10407 (O78:H11). The essential purification steps were membrane filtration (Millipore Corp.), ammonium sulfate fractionation, and negative diethylaminoethyl-Sephadex column chromatography. Yields were approximately 4.0 mg of **CFA**/I protein per g (wet weight) of bacteria. Purified **CFA**/I is a fimbrial molecule 7.0 nm in diameter and has an average molecular weight of 1.6 X 10(6), as determined by sedimentation equilibrium. **CFA**/I is a polymer of identical subunits of molecular weight 23,800 with an N-terminal valine, 37% hydrophobic amino acid residues, and 11 residues of proline per mol. The purified antigen retains its morphology, antigenicity, and biological activity. Purified antigen retains its morphology, antigenicity, and biological activity. Purified **CFA**/I exhibits mannose-resistant hemagglutination of human group A,

bovine, and chicken erythrocytes, as do **CFA**/I-positive bacteria. This was demonstrated by sensitizing latex microbeads with the purified antigen since cell-free **CFA**/I fimbriae do not hemagglutinate erythrocytes. Thus, **CFA**/I detached from the bacteria are monovalent; however, purified **CFA**/I antigen retains an affinity for the epithelial cells of rabbit small intestine and blocks adhesion of **CFA**/I-positive bacteria. These results demonstrate that purified **CFA**/I is a good candidate for use in an **oral vaccine** for immunoprotection against **diarrhea** caused by **CFA**/I-positive **enterotoxigenic** E. **coli**.

(FILE 'CAPLUS, MEDLINE, BIOSIS, EMBASE, WPIDS, JICST-EPLUS, JAPIO, PHIC, PHIN, TOXCENTER' ENTERED AT 10:55:21 ON 31 MAY 2002)

L17 197 S CARLIN N?/AU
L18 136 S ASKELOF P?/AU
L19 57 S BJARE U?/AU
L20 2 S L17 AND L18 AND L19
L21 5 S L17 AND (L18 OR L19)
L22 2 S L18 AND L19
L23 383 S L17 OR L18 OR L19
L24 4 S L23 AND L5
L25 6 S L20 OR L21 OR L22 OR L24
L26 4 DUP REM L25 (2 DUPLICATES REMOVED)

- Author(s)

L26 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 1

ACCESSION NUMBER: 2000:441654 CAPLUS
DOCUMENT NUMBER: 133:64009
TITLE: Oral vaccine against diarrhea
INVENTOR(S): **Carlin, Nils; Askelof, Per; Bjare, Ulf**
PATENT ASSIGNEE(S): SBL Vaccin AB, Swed.
SOURCE: PCT Int. Appl., 11 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000037106	A1	20000629	WO 1999-SE2306	19991209
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
SE 9804415	A	20000619	SE 1998-4415	19981218
SE 515285	C2	20010709		
BR 9916278	A	20010904	BR 1999-16278	19991209
EP 1140159	A1	20011010	EP 1999-964847	19991209
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
NO 2001002889	A	20010612	NO 2001-2889	20010612

PRIORITY APPLN. INFO.: SE 1998-4415 A 19981218
WO 1999-SE2306 W 19991209

AB An oral vaccine compn. against **enterotoxigenic** E. **coli** caused **diarrhea** in humans is disclosed. It comprises a defined amt. of at least three different types of colonization factor antigens (CFAs), e.g. 100 to 300 .mu.g of each type, selected from the group consisting of CFA I, CFA II (CS1, CS2 and CS3) and CFA IV (CS4, CS5 and CS6), on killed E. coli bacteria lacking the gene encoding the heat labile enterotoxin (LT-), together with a defined amt. of the B-subunit of cholera toxin (CTB), e.g. 0.5-2.0 mg, and a vehicle, such as PBS, which vaccine compn. is purified from possible heat stable enterotoxin (ST).

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L26 ANSWER 2 OF 4 MEDLINE
ACCESSION NUMBER: 2000156955 MEDLINE
DOCUMENT NUMBER: 20156955 PubMed ID: 10689236
TITLE: Double-blind, randomized, placebo controlled pilot study evaluating efficacy and reactogenicity of an oral ETEC B-subunit-inactivated whole cell vaccine against travelers' diarrhea (preliminary report).
AUTHOR: Wiedermann G; Kollaritsch H; Kundi M; Svennerholm A M; **Bjare U**
CORPORATE SOURCE: Institute for Specific Prophylaxis and Tropical Medicine, University of Vienna, Austria.
SOURCE: JOURNAL OF TRAVEL MEDICINE, (2000 Jan) 7 (1) 27-9. Journal code: C7W; 9434456. ISSN: 1195-1982.
PUB. COUNTRY: Canada
(CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(RANDOMIZED CONTROLLED TRIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200005
ENTRY DATE: Entered STN: 20000518
Last Updated on STN: 20000518
Entered Medline: 20000510

AB **Diarrhea** caused by **enterotoxigenic** E. **coli** (**ETEC**) is an important health problem in developing countries and in travelers to these areas. In previous trials formulations of ETEC vaccines containing the B-subunit of cholera toxin, which is antigenically similar to the heat labile enterotoxin of ETEC, and the most prevalent colonization factor antigens of ETEC, were shown to stimulate relevant mucosal immune responses in volunteers from Sweden and Egypt.

L26 ANSWER 3 OF 4 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1999:468494 BIOSIS
DOCUMENT NUMBER: PREV199900468494
TITLE: Method of cultivating bacteria proteins that are expressed in a temperature regulated manner.
AUTHOR(S): **Askelof, Per; Carlin, Nils;** Nilsson, Bo; Paulsson, Agneta
CORPORATE SOURCE: Department of Clinical Research, Merck Sharp and Dohme (Sweden) AB, SE-192 07, Sollentuna Sweden
ASSIGNEE: SBL Vaccin AB

PATENT INFORMATION: US 5935838 Aug. 10, 1999
SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (Aug. 10, 1999) Vol. 1225, No. 2, pp. NO PAGINATION.
ISSN: 0098-1133.
DOCUMENT TYPE: Patent
LANGUAGE: English

L26 ANSWER 4 OF 4 WPIDS (C) 2002 THOMSON DERWENT
ACCESSION NUMBER: 1996-058138 [06] WPIDS
DOC. NO. CPI: C1996-019280
TITLE: Temp. regulated cultivation of bacteria expressing surface antigens - for improved prodn. of bacteria for use in prepn. of oral vaccines against e.g. E.coli.
DERWENT CLASS: B04 D16
INVENTOR(S): **ASKELOF, P; CARLIN, N;** NILSSON, B; PAULSSON, A; ASKELOEF, P
PATENT ASSIGNEE(S): (SBLV-N) SBL VACCIN AB
COUNTRY COUNT: 65
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9533825	A1	19951214	(199606)*	EN	11
RW: AT BE CH DE DK ES FR GB GR IE IT KE LU MC MW NL OA PT SD SE SZ UG					
W: AM AU BB BG BR BY CA CN CZ EE FI GE HU IS JP KG KP KR KZ LK LR LT LV MD MG MN MX NO NZ PL RO RU SG SI SK TJ TM TT UA UG US UZ VN					
AU 9526349	A	19960104	(199613)		
EP 759981	A1	19970305	(199714)	EN	
R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE					
JP 10501406	W	19980210	(199816)		13
US 5935838	A	19990810	(199938)		
MX 9606032	A1	19980501	(200007)		
MX 195832	B	20000403	(200124)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9533825	A1	WO 1995-SE628	19950601
AU 9526349	A	AU 1995-26349	19950601
EP 759981	A1	EP 1995-921214	19950601
		WO 1995-SE628	19950601
JP 10501406	W	WO 1995-SE628	19950601
		JP 1996-500754	19950601
US 5935838	A	WO 1995-SE628	19950601
		US 1997-750509	19970421
MX 9606032	A1	MX 1996-6032	19961202
MX 195832	B	MX 1996-6032	19950601

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9526349	A	Based on	WO 9533825

EP 759981 A1 Based on WO 9533825
JP 10501406 W Based on WO 9533825
US 5935838 A Based on WO 9533825

PRIORITY APPLN. INFO: SE 1994-1921 19940603
AN 1996-058138 [06] WPIDS
AB WO 9533825 A UPAB: 19960212
A method of cultivating bacteria contg. plasmids comprising genes encoding surface or membrane-bound antigens or other proteins which are expressed in a temp. regulated manner for the prodn. of desired bacterial prods. is characterised in that (a) the bacteria are first cultivated in a medium at a temp. such that the bacteria retain their plasmids but no expression occurs; then (b) the inoculum is further cultivated in a medium at a temp. at which expression occurs, the bacteria being harvested before they lose the plasmids; and then (c) the desired prod. is isolated.

USE - Commercial quantities of E.coli bacteria with intact colonisation factor antigens (CFAs) and their sub-components (CS antigens) can be produced in large scale industrial fermenters. The bacteria can be inactivated with formalin and then used to prepare oral vaccines against E. coli.

ADVANTAGE - In previous attempts to scale up the prodn. of E. coli bacteria having CFAs it was found that the bacteria lost their ability to produce the CFAs more and more for each new generation. This was found to be due to the loss of the temp. regulatory gene localised in a plasmid in the bacteria. Regulation of the temp. as described above resulted in increased yields of the bacteria.
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